# SCIENCE

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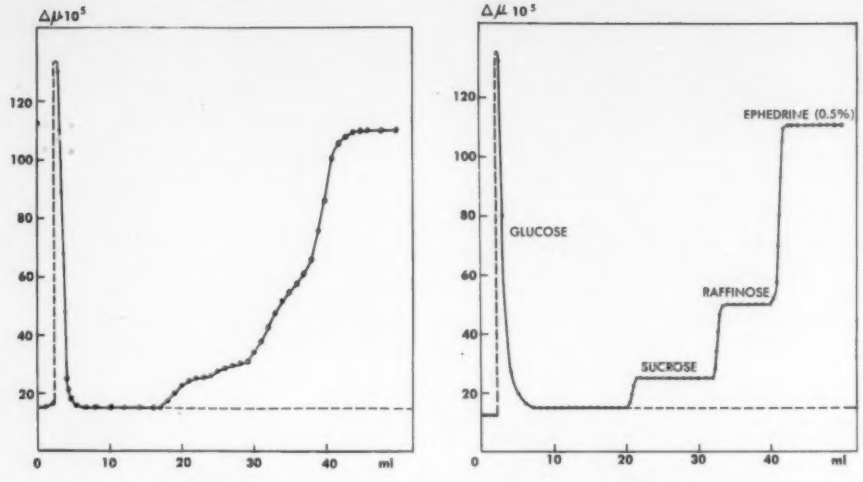


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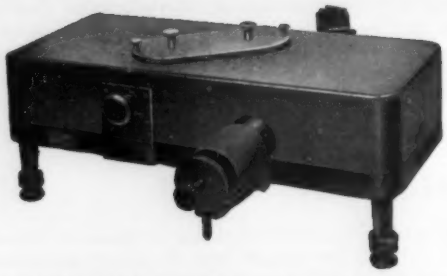

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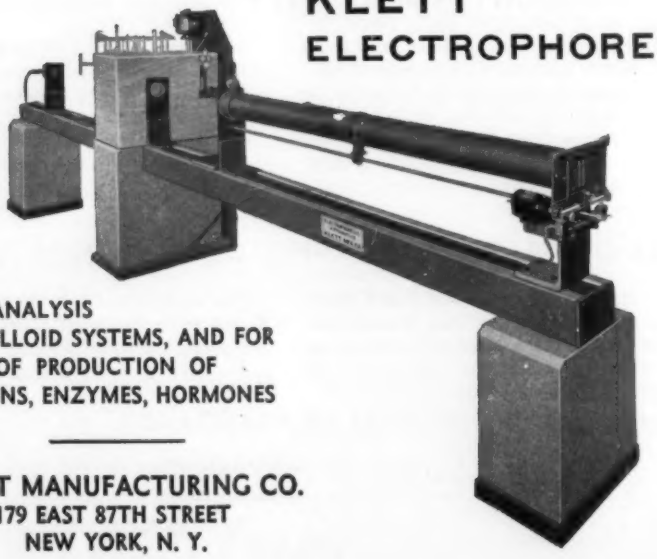

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## New Directions in Research Support

The board of directors of the American Cancer Society has recently approved a bold approach to the problem of support of research and investigators in cancer research. Although the usual project and contract modes of support will be continued, the society has added "program grants" that will permit "freely roaming inquiries into specific areas that have been judged to be of significance to the cancer problem." This approach will permit continuity of support to exploratory work in research and will free the investigator from the all-too-familiar pressure of looking for problems that will yield quick results in order to justify renewal of an annual grant. The program does much of what W. M. Stanley called for in a recent editorial [*Science* **123**, 353 (2 Mar. 1956)].

The society has taken a refreshingly realistic look at the requirements for successful scientific exploration and recommends that "the investigator must have freedom to change the direction and emphasis of his investigation . . ." and that he ". . . must be allowed considerable latitude in expending funds." This seems to us to be an enlightened policy that may well stimulate other fund-granting institutions to liberalize the conditions of their grants.

The society departs even further from traditional practice in its proposal to make grants to institutions that will permit them to create additional permanent faculty-level positions. Each grant will provide a capital fund of about $200,000. This will make possible the creation of one additional suitable position for one investigator with salary from the age of 31 through 65, at the rate of $6000 for each of the first 3 years with a gradual rise to $15,000 for the last 17 years.

Both of these steps—the support of a flexible program over a long term and the allocation of funds to create a suitable permanent position for an investigator through the major part of his productive career are eminently practicable departures from current practice. Inasmuch as several new permanent posts will be created every year over a period of years, the ultimate effect will be large.

An additional forward-looking step of considerable significance is the society's decision to make grants of fluid funds—"institutional research grants"—to institutions to provide "grub-stakes" to support the preliminary testing of new and venturesome ideas for research on cancer. It is proposed that such funds be expended with the advice of a committee of scientists within the grantee institution. The continuation of such grants will be dependent on how well the previous grant was expended rather than on proposals for future research that may or may not be pursued. This innovation will constitute a considerable challenge to the local scientific advisory committee that must function with integrity, alacrity, and imagination.

If the program in support of research were narrowly conceived, we would have some reservation about its wisdom. Fortunately, however, cancer research is broadly defined to include fundamental research in the physical and biological sciences.

This new approach to the support of research by the American Cancer Society is no less important than similar steps taken by the Commonwealth Fund and the Ford Foundation in the closing months of 1955. Could it be that we are witnessing the dawn of a new era when granting agencies are accepting more of their ultimate responsibilities? If so, scientists should be aware that if they accept these broadened opportunities they also accept commensurate responsibilities for accelerated scientific progress.—G. DUS.

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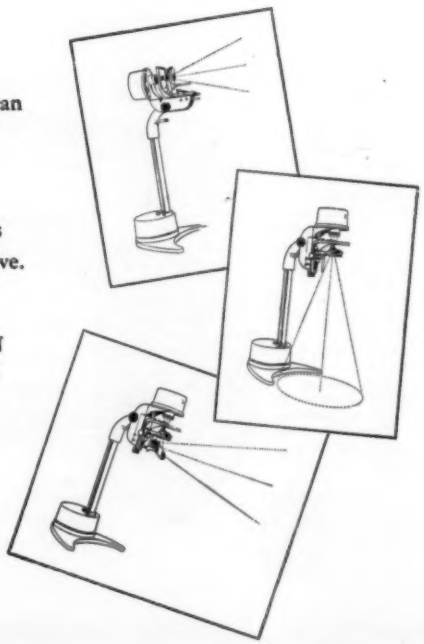

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# Biology of Inflammation

## Chemical Mediators and Cellular Injury

Valy Menkin

Inflammation is a manifestation in vertebrates of severe cellular injury, and as such it represents the basis of all infectious processes. It can readily be defined as the complex vascular, lymphatic, and tissue response on the part of vertebrate tissue to the presence of an irritant. An irritant may be considered to be any agent that interrupts normal cellular metabolism. It may be physical in nature, or chemical, or viable, as in the case of microorganisms.

Inflammation consists of a number of interdependent sequences that lead to the localization and ultimate disposal of the irritant. These phases are often grouped under the somewhat loose term *inflammatory reaction*. Initially, there is a disturbance in fluid exchange, which is manifested by an alteration in the normal equilibrium of capillary filtration. There is at first, as shown by Landis, a transitory increase in capillary pressure (*1*), and this is followed by more permanent changes in the structure of the endothelial wall structure—namely, augmentation in its permeability (*2*). For instance, the enhancement in permeability can be readily demonstrated by introducing trypan blue into the circulating blood of a rabbit. The area of injury is rapidly stained, owing to the outward passage of the dye (*3*). The magnitude of increase in permeability is such as to allow particulate material to pass into the extracapillary spaces (*4*). The extent of increased capillary permeability is subject to measurement. In 1930 it was shown that, when a dye is introduced into the ventricle of a pithed frog with its mesenteric capillaries exposed on the stage of a microscope, one can evaluate with an appropriate scale the rate of change of concentration of the dye as it passes out into the extracapillary spaces. It was then found that with inflammation caused by certain irritants, the permeability of capillaries is enhanced about twofold (*3*).

### Leukotaxine and the Mechanism of Increased Capillary Permeability

The mechanism of increased capillary permeability in inflammation is an important factor, for it is the pivotal reaction on which all subsequent sequences depend. In 1924, Lewis, stimulated by the work of Ebbecke, postulated that the phenomenon is referable to the liberation of histamine or at least to a substance so closely allied to it that he termed it the "H-substance" (*5*). The argument utilized by Lewis is fraught with difficulty, for it is largely one of analogy. For this reason, I reinvestigated the whole problem in 1936 (*6*). It was readily shown that the exudative fluid recovered from the site of inflammation contains a factor that is capable of eliciting an increase in capillary permeability. Subsequently, chemical extraction was undertaken and a crystallinelike material was isolated. This substance is capable of increasing the permeability of capillaries with inflammation. It has been called leukotaxine (*7*).

Cullumbine and Rydon, Pasquali, and Morimoto have confirmed the isolation of this chemical substance (*8–10*). It is evidently not a protein. It has an α-amino group and an indole nucleus. There is evidence that it is a polypeptide to which some as yet unknown prosthetic group may be attached. The substance today, even though it is not chemically pure, appears definitely to be a chemical entity (*11*). It has marked biological specificity (*11*). Chromatographic studies, undertaken by my associate W. Kalnins, indicate the presence of at least five distinct amino acids (leucine, valine, α-alanine, glycine, and glutathione). Aspartic acid and glutamic acid appear as a fused unit in the chromatogram (*11*).

It has none of the properties of histamine, thereby throwing considerable doubt on the view of Lewis that the H-substance is primarily concerned in the mechanism of increased capillary permeability in inflammation (*5*).

The increase in capillary permeability induced by leukotaxine has been found to be counteracted by only one substance—namely, the extract of the adrenal cortex—and to be counteracted to a certain extent by some of the compounds derived from the adrenal cortex —namely, cortisone and hydrocortisone. This phase will be discussed subsequently.

Leukotaxine is concerned with another fundamental manifestation in inflammation—namely, the migration of polymorphonuclear leukocytes to the site of injury. This is referred to as "chemotaxis *in vivo*" (*11, 12*). Leukotaxine does not as yet explain the exact intrinsic cellular mechanism concerned in the motion of leukocytes, but it at least stands out as a concrete substance, liberated in exudates, that is definitely chemotactic. This fact in itself offers a distinct possibility for attacking the problem further in an endeavor to determine how leukotaxine specifically affects the mobility of white cells so as to induce their migration to the site of inflammation. Whether electric charges have anything to do with the phenomenon remains to be proved. The end product of blood serum extracted for leukotaxine yields no activity as far as cell migration is concerned. On the other hand, leukotaxine derived from exudates is definitely chemotactic, for its injection into tissues induces (within 13 to 14 minutes with some fractions) not only a marked increase in capillary permeability but also a distinct migration of polymorphonuclear cells outward into the area of injury (Figs. 1 and 2). The

The author is head of the Agnes Barr Chase Foundation for Cancer Research, Temple University School of Medicine, Philadelphia, Pennsylvania.

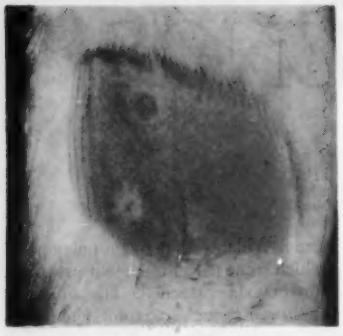

Fig. 1. Effect of leukotaxine extracted from an exudate (with the utilization of 1*N* acetic acid in the final analysis) on capillary permeability in the dermis of the abdomen of a rabbit. Six milliliters of 1-percent trypan blue in saline was injected intravenously. Note the accumulation of the dye within 25 minutes in the upper area owing to the increase in capillary permeability caused by leukotaxine. No such effect is elicited by the mere injection of saline (lower area).

chemotactic property of leukotaxine can be easily demonstrated by *in vitro* observations. The placing of leukotaxine on a slide containing a drop of exudate is soon followed by orientation, migration, and clustering of cells at the periphery of particles of leukotaxine. No such effect is observed with either carbon particles or reduced iron powder (*4, 11, 12*).

In conclusion, leukotaxine extracted from inflammatory exudates offers a reasonable explanation for two of the basic sequences in inflammation—namely, the primary mechanism of increased capillary permeability and the local migration of polymorphonuclear leukocytes. Besides these two functions, leukotaxine appears to be relatively innocuous as far as the induction of any appreciable degree of tissue injury is concerned.

## Role of Inflammation in Immunity

Concomitantly with the increase in capillary permeability, induced primarily by leukotaxine, which is released in turn by injured cells at the site of an acute inflammation, there follows the rapid passage from the circulation of the plasma proteins into the area of injury. These are in order of magnitude: the albumin, globulins, and fibrinogen. In the presence of thrombokinase, the latter is precipitated out as a fibrinous network in tissues, now distended with edema. The lymphatic channels, which drain the particular area, are apparently more delicate in structure than capillaries and are therefore more readily damaged. They become filled with fibrinous plugs or thrombi. A true lymphatic blockade ensues. Material injected into such a "walled off" or circumscribed area is incapable of escaping through the lymphatics. Such material is mechanically fixed at the site of the acute inflammation owing to a blockage of lymphatics and the presence of a fibrinous network (*4*).

These observations have been extended to the problem of bacterial invasiveness. The rapidity and intensity through which lymphatic blockade is established in an inflamed area serve as a gage of the invasiveness of a microorganism—that is, if such a viable vector happens to be the irritant. Microorganisms disperse from their point of inoculation via lymphatics. In this way it was shown that staphylococci are localizing microorganisms largely because of their marked injurious effect on tissue at their point of entry. There then results the rapid establishment of a lymphatic blockade. On the contrary, the hemolytic streptococci produce a relatively mild local reaction. The lymphatics are maintained patent for as long as 2 days, thus allowing the microorganisms to disseminate freely.

One is dealing with a paradox. The streptococci are feared microbes, whereas the reverse is usually held for the ubiquitous staphylococci. This is primarily due to the potent lethal effect and the prompt establishment of a lymphatic blockade by the staphylococci at their point of entry. The streptococci, on the other hand, are harmful to the organism as a whole owing to their unhindered dispersive capacity through patent lymphatics (*13*). In this way it is seen that, from the standpoint of immunity, an acute inflammation is the regulator of bacterial invasiveness (*14*). One can formulate this concept as follows: $D = Kt/I$, where $D$ refers to dissemination from the point of entry, $I$ is the degree of induced local injury and $t$ refers to time; $K$ may be considered a constant that refers to the type of irritant and the anatomical location of the lesion. In other words, the invasiveness of a microorganism is to a large extent inversely related to the intensity of the local injury it induces (*4, 14*).

The fixation or localization described, which is referable to lymphatic blockade, is also an important principle. With some irritants, the "walled off" process occurs within 30 minutes after the injection of an irritant. This rapidity allows a definite interval for the irritant to be circumscribed and for the sluggish leukocytes to assemble for phagocytosis (*4, 15*).

Finally, the capillaries eventually likewise become occluded by thrombi. The inflamed area then becomes, so to speak, isolated from the rest of the organisms. It develops its own $\phi$H, metabolism, and local circulation. Prior to this type of local insulation, in which one may envisage that the organism is protected at the expense of local injury, various inert materials or bacteria that have been intravascularly injected concentrate in the area of acute inflammation because of the initial increased local capillary permeability and the early simultaneous establishment (with some types of irritants) of a lymphatic blockade (*4*).

The foregoing immunological view is of the utmost importance in our understanding of inflammation in its role in immunity. This, in the last analysis, is the most important aspect of inflammation in body organization.

## Mechanism of Leukocytosis with Inflammation

The leukocytosis-promoting factor is another potent biologic substance that was isolated in 1940 from the site of inflammation (*16*). Leukotaxine introduced into the circulating blood fails to alter the number of white cells. Yet it is well known that in numerous inflammatory processes the level of circulating leukocytes is considerably elevated. The leukocytosis has been shown to be referable to chemical units. The injection of whole exudative material derived from a

Fig. 2. Forty-four minutes after the introduction of leukotaxine into the cutaneous tissue of a rabbit. The material injected was crystallinelike in nature. It also induced a markedly increased capillary permeability. Note that the capillary lumen is crowded with polymorphonuclears actively migrating into the extracapillary spaces. (About × 350.)

dog with a concomitant leukocytosis into the blood stream of a recipient dog induces a prompt leukocytic response. Neither leukotaxine nor blood serum is capable of eliciting such a response. The evidence indicates that there is a leukocytosis-promoting factor present in inflammatory exudates. This factor, in contrast to leukotaxine, is nondiffusible through a cellophane membrane and it is destroyed by heat at 60°C. Its injection is accompanied by a discharge of immature leukocytes into the circulation. Chemical extraction of exudates yields activity in the pseudoglobulin fraction (*17*). Cataphoretic studies with a Tiselius apparatus indicate that the leukocytosis-promoting factor (LPF )is distributed between the alpha$_1$ and alpha$_2$ globulins of exudates (*18*). Other protein fractions, such as the albumin and the euglobulin, are ineffective in inducing a state of leukocytosis. The material is absent in normal blood serum, but it can be recovered from the serum of an animal with a concomitant inflammation (*19*). This fact suggests that it reaches the bone marrow by way of the blood stream. The material can be obtained from the exudates of dogs, of rabbits, and of human beings (*20*).

The leukocytosis-promoting factor not only discharges immature granulocytes into the circulation but also induces a marked and specific growth in the bone marrow (*21*). The result is a conspicuous hyperplasia of some of the hematopoietic cells, notably the polymorphonuclear leukocytes and the megakaryocytes (Fig. 3).

In brief, the leukocytosis-promoting factor of exudates offers a reasonable explanation for the mechanism of leukocytosis that accompanies numerous inflammatory processes. Its marked growth effect on some of the elements of the bone marrow may prove to have clinical implications. In fact, it has been shown that the canine material can be injected innocuously into human beings, in whom it likewise increases the white counts (*22*). The active group in the pseudoglobulin molecule has been shown to be due to a polypeptide (*23*). The factor also enhances the ordinary leukocytosis caused by an inflammation. This suggests the possible use of this substance on patients with various inflammatory disorders (*24*). There is another thermostable leukocytosis-promoting factor liberated in acid exudates that will be discussed briefly in a subsequent paragraph.

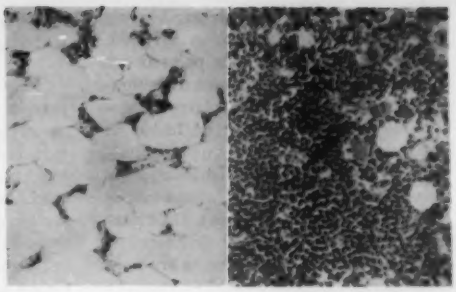

**Fig. 3. (Left) Femoral bone marrow of a dog 2 days following an injection of 14.5 milligrams of pseudoglobulin derived from normal blood serum. There is clearly no evidence of any hyperactivity. (Right) Femoral bone marrow of a dog 2 days following a single injection of 13.5 milligrams of the leukocytosis-promoting factor. The hyperplasia is striking. (× 165) [From V. Menkin, *Am. J. Pathol.* 19, 1021 (1943)]**

## Cytologic Sequence in Inflammation

Another fundamental sequence in the development of the inflammatory reaction is the initial infiltration of polymorphonuclear leukocytes, which are subsequently replaced by macrophages. This is an almost invariable cytologic sequence. With some irritants, the polymorphonuclear phase may be lengthened and the macrophage phase correspondingly shortened—for example, a staphylococcal abscess, or, vice versa, a tubercle. Nevertheless, the same basic principle is maintained. In 1934 it was observed that this phenomenon is referable to a developing local acidosis at the site of an acute inflammation (*25*). It was demonstrated in 1931 that the local circulation in an inflamed area is markedly impaired. The lymphatic outlets become occluded (*26*), and in time thrombi are also found in the smaller vascular channels.

Thus, as stated in a preceding section, the area of inflammation becomes more or less isolated from the rest of the organism. It has already been pointed out that it develops its own hydrogen-ion concentration, its own circulation, and its own metabolism. The polymorphonuclear leukocytes brought to the site of injury primarily through the action of leukotaxine, as described, are unable to survive below a *p*H of 7.0, whereas the mononuclear phagocytes appear fairly normal at *p*H 6.9 to 6.8. At a somewhat lower *p*H all types of leukocytes tend to be injured. The result is a state of suppuration. Pus in acute inflammation is virtually a function of the hydrogen-ion concentration (*4*). For instance, a 24-hour exudate from the pleural cavity of a dog that has previously been injected with turpentine is primarily composed of polymorphonuclear leukocytes, whereas an exudate of several days' duration at *p*H 6.5 reveals an absence of normal polymorphonuclear cells. The rise in hydrogen-ion concentration tends to precede the change in the differential leukocyte picture (*25*).

On the other hand, if the reaction remains alkaline during the development of the inflammatory reaction, the cellular picture is characterized throughout by a predominance of polymorphonuclear leukocytes. That the general effect is an inability on the part of polymorphonuclear leukocytes to survive at an acid reaction has been demonstrated by subjecting leukocytes *in vitro* to buffers at various hydrogen-ion concentrations (*27*). In this way, it was readily shown that these cells tend to cluster and become swollen with coarse granulation at about *p*H 6.5. When they are supravitally stained, the nuclei take up the dye, indicating severe injury. These changes are absent in cells exposed to *p*H 7.4. It should be mentioned that this relationship does not apply in rabbits (*28, 29*). This may be referable to the absence or reduction of proteolytic enzymes in the leukocytes of this animal (*28, 30*).

It is important to determine the mechanisms of local acidosis in inflammation if one is to comprehend the forces at work in forming the cytologic picture at the site of an acute inflammation. The alkali reserve of the exudate tends to decrease with the developing local acidosis (*28*). This in itself might be expected to occur, for it is another means of expressing the rise in hydrogen-ion concentration. Incidentally, it is well to emphasize again that all the biochemical changes are local: the reaction of the blood remains essentially unaltered.

The local acidosis seemed to be primarily referable to a glycolytic process (*28*). The result was a true lactic acid acidosis. Several chemical variables had been studied in the exudate during the progress of the inflammatory reaction. These included the concentration of sugar and of lactic acid and the measurement of the *p*H, correlated in turn with the cellular picture. The conversion of glucose to lactic acid induced a local acidosis, with the resulting effect on the leukocytes that has been described.

In conclusion, the cellular picture or the survival of leukocytes in inflammation is primarily conditioned by the hydrogen-ion concentration, which in turn seems to be referable to a disturbance in the intermediary carbohydrate metabolism. The lymphocytes appear to be unaffected, at least directly, by the changes in hydrogen-ion concentration. The function of the latter cells is still somewhat obscure. The studies of McMaster and Hudack and the more recent

work of Harris suggest their possible role in the formation of antibodies (*31, 32*). Maximow and Bloom have pointed out that in inflammatory exudates transitions from the lymphocytes to the large phagocytosing macrophages can be found in great number (*33*). Finally, recent studies *in vitro* indicate that leukotaxine is likewise chemotactic to mononuclear phagocytes (*11*). This phase will be particularly significant if it can be shown to occur also *in vivo*. Such studies are now in progress.

### Diabetes and Inflammation

The biochemical studies on the relationship of the hydrogen-ion concentration to the cellular picture at the site of an acute inflammation have led to further extensive investigation in an attempt to unravel the mechanism concerned in the intensifying of the diabetic state when there is a superimposed inflammation in diabetic dogs (*34*). An inflamed area is a focus of proteolysis. At the site of inflammation in a diabetic animal, the breakdown of proteins is considerably exaggerated.

Local sugar formation from the split part of the protein molecule by deamination readily explains the heightening in blood sugar following the diffusion of sugar previously formed at the site of injury. Close analysis indicates that, in general, even in nondiabetic animals, sugar can be formed by injured cells. Such cells are therefore potentially foci of gluconeogenesis (*35*). The process is merely exaggerated in the diabetic animal, and furthermore, there is an absence of insulin. There is also some suggestive evidence that urea, besides originating in the liver, is possibly formed at the site of an acute inflammation (*35*).

Studies performed in 1946 indicate that there is another toxic substance liberated at the site of injury, termed "necrosin," which by itself is also capable of heightening somewhat the level of blood glucose, presumably by releasing the latter from the liver (*36*). Thus, the state of diabetes complicated by inflammation appears to be reinforced by the formation of glucose locally from the injured cells and also perhaps by the release of sugar from the liver through the effect of necrosin (*36*). The aspect of carbohydrate metabolism and its possible relationship to inflammation has been treated critically and at greater length elsewhere (*12*). The possible additional participation in the mechanism concerned of various endocrine structures, such as the adrenal cortex, the pituitary, or the thyroid, has been considered and, therefore, requires further study (*12, 34*).

### Chemical Basis of Injury in Inflammation

The fundamental stereopattern of injury in the development of the inflammatory reaction, irrespective of the irritant, is of great importance. The irritant and anatomic location of the lesion may modify the ultimate appearance. Nevertheless, close scrutiny reveals a basic pattern of injury, as manifested by the cardinal signs of inflammation described by Celsus at the beginning of our era. In addition, damaged cells may show granular elements strewn through their cytoplasm; the cells may be vacuolated; the collagenous bundles may appear to be swollen; and the nuclei may reveal various degrees of shrinkage. Another evidence of tissue injury found in a variety of acute inflammatory lesions is displayed by the fibrinous occlusion of lymphatics and also by the presence of small thrombi in the blood vessels of an inflamed area.

It may be asked whether the mechanism that accounts for the basic pattern of injury in inflammation is referable to a chemical unit. Leukotaxine scarcely induces any degree of injury to cells except for an augmentation of cellular permeability. The leukocytosis-promoting factor elicits essentially no injury to tissues. Studies in 1943, however, have indicated that the euglobulin fraction of exudates is highly injurious to the cutaneous structures of the rabbit and to some extent to those of the dog (*37*). There is thus an accumulated body of evidence that, either in the euglobulin fraction of particularly acid exudates or else associated with it, there is present an injury factor that is capable per se of reproducing the nocuous effects seen in inflammation. This substance or factor has been termed "necrosin" (*37*). Its injection into the skin of rabbits is accompanied by intense redness, edema, and usually a central area of necrosis (Fig. 4). No other fractions of exudate appear to be capable of inducing any such severe effect. Furthermore, the euglobulin fraction of normal blood serum elicits absolutely no appreciable lesion in the skin of rabbits. On the other hand, the same fraction from the serum of a dog with a concomitant acute pleural inflammation may induce a severe inflammation. This observation suggests that the toxic substance is absorbed from the site of inflammation into the circulation, from which it can be recovered. This fact is perhaps of significance in reevaluating the concept of a focus of infection and its far-reaching repercussions on other organs.

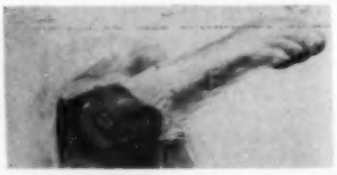

Fig. 4. Effect of necrosin injected into the skin of the foreleg of a rabbit. The acute inflammatory reaction with areas of central necrosis is about 1 day old. The necrosin was obtained from a dog's exudate. [From V. Menkin, *Arch. Pathol.* 36, 269 (1943)]

Necrosin induces an acute inflammation with blockade of the lymphatics. A section through such an area reveals zones of dense leukocytic infiltration in which the lymphatic channels may be occluded by thrombi. Small vascular channels may also show evidence of clot formation. On the other hand, the euglobulin fraction of normal serum leaves the lymphatic channels essentially patent. About 10 minutes after the injection of necrosin into the skin of rabbits, the connective tissue bundles occasionally appear to be swollen, with a tendency to fuse together. The latter seems to be one of the first morphologic evidences of the injurious effect of necrosin on supporting structures (*37*).

As stated previously, necrosin can at times be recovered from the blood serum of an animal with an acute inflammation. This interesting observation, which may reasonably explain the toxic effect of a lesion on organs at a distance, has suggested the necessity for examining the generalized effect on organs following an intravascular injection of necrosin. Although several organs, such as those in the gastrointestinal tract, may show evidence of injury, or various lymphoid structures may reveal signs of enlargement and congestion, it is nevertheless only the liver and to some extent the kidneys that seem most frequently to show signs of damage. Many of the cells of the liver appear swollen and are laden with fat. The liver on gross examination is streaked with what seems to be yellowish or whitish foci. In some cases, the cell outlines have disappeared and the liver cords are stippled with coarse, black-stained granules that do not take the iron stain. The epithelial lining of the kidney tubules may show irregularities and vacuolation, and foci of leukocytic infiltration, separating some of the tubular structures, may also be present (*22, 37*). Perhaps it should be pointed out that the various injurious biological effects obtained by ionizing radiation may well prove to be referable to the liberation of necrosin, as well as to some of the other factors, by cells that are injured, in this case, by a physical irritant.

There are two additional properties of the euglobulin fraction of acid exudates that indicate its significance to the

student of pathology. The intravascular injection of this fraction into a dog may be accompanied by severe toxic manifestations, including vomiting and diarrhea. For a while the animal lies on its side and appears somewhat prostrated. Of greater significance is the abrupt fall in the number of circulating leukocytes, which is usually extremely marked. The white cell count may fall in an hour or two from about 10,000 to 1000 or 2000 per cubic millimeter. After several hours the dog appears to be clinically improved, and the white cell count rises. Subsequently, or on the following day, a leukocytosis may ensue. This leukocytosis, associated with the euglobulin of particularly acid exudates, has been shown to be referable to a thermostable leukocytosis-promoting factor. The mechanism of leukocytosis with inflammation is thus ascribed to at least two factors that are liberated by injured cells: (i) the thermolabile leukocytosis-promoting factor, (LPF), and (ii) a thermostable leukocytosis factor (*38, 39*).

On the other hand, as just pointed out, the depression in the number of circulating leukocytes or the state of leukopenia is also referable to two factors: (i) a leukopenic factor associated with the euglobulin of acid exudates (*40*) and (ii) leukopenin recovered in the pseudoglobulin fraction (*41*). Leukopenin is recovered in abundance from aged LPF (*41*) and it appears to be present in alkaline exudates (*41*).

It is difficult to predict accurately the number of circulating leukocytes when there is a concomitant acute inflammation. This indeterminate status is due to the fact, as just pointed out, that there are four factors involved. Two factors cause an elevation in the level of circulating leukocytes (LPF and the thermostable leukocytosis factor), and two factors induce a decrease in the level of white cells (leukopenin and the leukopenic factor). The ultimate level of leukocytes in the blood stream is a resultant of the interrelationship of these four factors (*12, 42*).

Of perhaps even greater interest is the fact that the intravascular injection of the euglobulin fraction of acid exudates in dogs is often accompanied by a marked rise in temperature simultaneously with the developing leukopenia, possibly of 3° to 5°F. The studies of Grafe in 1910 suggested that in infectious processes the fever is referable to the absorption of products of cellular disintegration. Other protein fractions of exudate—for example, the leukocytosis-promoting factor or the euglobulin fraction of normal serum —are incapable of inducing any fever when they are injected into the circulating blood of a dog. The fact that the euglobulin fraction of acid exudates seems to be the only fraction that has this capacity suggests strongly its possible role in the production of fever with inflammation (*37*).

In 1945 I succeeded in dissociating from the euglobulin fraction of exudates the fever-causing factor (*43*). I called this fever-inducing substance "pyrexin." Pyrexin seems to give a reasonable explanation for the development of fever with inflammation. It seems to be a protein split product, a polypeptide, to which there seems to be attached a carbohydrate group. It is quite possible that the latter group is associated with the thermostable leukocytosis factor; but this requires further study (*38, 39, 42*). Pyrexin was brought to the crystalline state in 1952 (*44*). There is no factual or experimental evidence that pyrexin is a contaminant by bacterial pyrogens. On the contrary, all available evidence indicates that pyrexin is a direct product of cellular injury, which is recovered particularly in acid exudates (*12, 45, 46*).

## Anti-inflammatory Problem

In 1940 a report was made on the suppressing effect of whole adrenal cortical extract on the increased capillary permeability caused either by whole exudate or by leukotaxine (*47*). In 1942 the same repressing effect was found with cortisone (compound E) (*48*). These were the first observations on the anti-inflammatory capacity of cortisone.

Following the studies of Kendall, Hench, and their collaborators on the effect of cortisone on arthritis, these studies were resumed in 1951 (*49–51*). The earlier observations were confirmed. However, an interesting difference was also found. Whereas an alkaline exudate or its contained leukotaxine was repressed by whole adrenal cortical extract or cortisone, an acid exudate was incapable of being repressed by either adrenal cortical extract or by cortisone. As a consequence, it was found that at the stage of development when the inflammatory reaction is at an acid level (but independently of the *p*H of the exudate) another chemical factor appears to be liberated by the injured cells. This substance, like leukotaxine, is also capable of increasing capillary permeability, but only in the later stages of inflammation. This factor has been termed "exudin" (*50*). In contrast to leukotaxine, which increases capillary permeability in the earlier stages and induces the emigration of polymorphonuclear leukocytes to the site of inflammation, exudin does not cause any appreciable migration of the cells through the endothelial wall of the capillaries. Exudin contains about 10 percent nitrogen. It can be obtained after first discarding the euglobulin fraction of acid exudates and then following with repeated reprecipitation of the pseudoglobulin-albumin fraction at one-third saturation of $(NH_4)_2SO_4$. Leukotaxine is suppressed by either adrenal cortical extract, cortisone, or hydrocortisone (compound F). On the other hand, none of these corticosteroids inhibit exudin. But ACTH or corticotropin suppresses exudin (*51*). There are thus two components throughout the duration of an acute inflammation which increase capillary permeability, namely leukotaxine and exudin. These two components can be distinguished from each other by their differing reactions with some anti-inflammatory agents. These facts can be briefly summarized as shown in Table 1.

Table 1. Reactions of leukotaxine and exudin and some anti-inflammatory agents: 0 indicates suppression of capillary permeability to trypan blue; + indicates no effect on the increased capillary permeability to trypan blue.

| Component | Adrenal cortical extract | Cortisone or Cpd. F | ACTH |
|---|---|---|---|
| Leukotaxine | 0 | 0 | + |
| Exudin | + | + | 0 |

The effect of ACTH or corticotropin in repressing exudin is a direct one, for the same response can be elicited in adrenalectomized rats (*52*). This observation does not controvert the classical physiological effect of ACTH on the adrenal cortex in releasing hydrocortisone or compound F, but the local inflammatory reaction can be envisaged as a sort of sieve with a very extensive increase in local capillary permeability. As a consequence, the injection of ACTH into the circulation of the animal induces a certain amount of seepage of this substance into the inflamed focus, with subsequent direct action on the exudin that is liberated in turn by the injured cells. Recent and as yet unpublished observations with pure ACTH in the form of α-corticotropin, obtained through the kindness of Choh Hao Li, corroborate further the direct effect of ACTH with now this single chemical entity. α-Corticotropin represses in an inflamed area the increased capillary permeability referable to either an acid exudate or exudin. This study tends to obviate the possibility of an impurity in the commercial ACTH to explain the earlier results.

The mechanism involved has also been studied. The mechanism of an anti-inflammatory steroid, namely hydrocortisone or compound F, seems to be at a cellular level. Cell activity is suppressed. In the sea urchin ova, as an isolated sys-

tem, cell division, following fertilization, is utilized as a criterion of cellular activity (*53*). It is shown that cortisone, compound F, and ACTH reduce the incidence of cell division, whereas neither testosterone propionate as a control for the steroids nor somatrofin (STH) as a control for another anterior pituitary hormone has any effect in altering the pattern of cell division (*53*). More recent studies (in 1954) reinforce further the view of suppressed cell activity, for it has been shown that cortisone and ACTH significantly retard the rate of cleavage in sea urchin ova (*Arbacia punctulata*) (*54*). It has also been demonstrated that the permeability to water of these isolated marine eggs is definitely reduced by an average of 34 percent after preliminary exposure to cortisone (*55*).

These findings of suppression of normal cell activity have been transferred to a study of the mechanism of an anti-inflammatory steroid in the dog (*56*). The activity of the injured cell at the site of an acute inflammation is likewise suppressed. The formation of the chemical factors responsible for the inflammatory reaction appears to be inhibited. Repeated injections of compound F (hydrocortisone) into an inflamed area suppresses the activity of leukotaxine and the leukocytosis-promoting factor. In the case of the latter substance, at least, it is shown by *in vitro* studies that the corticosteroid does not interact directly with the LPF, but that it evidently suppresses its formation by the injured cell. Therefore, here likewise the mechanism seems to be at a cellular level. Compound F (hydrocortisone) is an anti-inflammatory substance because it represses the injured cell from forming the very chemical substances concerned in the development of inflammation (*11, 56*).

The anti-inflammatory corticosteroids are actually harmful and therefore contraindicated in numerous infectious lesions—for example, tuberculosis and poliomyelitis. It seems that cortisone, by doing away with the chemical factors liberated in an inflamed area, allows free rein for microorganisms to proliferate and thus accentuates the pathological lesions caused by the microbes. It is probable that the anti-inflammatory agents should primarily be employed in noninfectious forms of inflammation. They are also of value in various eye infections, which, if not interfered with, may be complicated eventually by corneal opacities (*57*).

## Homeostasis in Inflammation

Homeostasis, as is well known, is a term coined by Walter B. Cannon in 1929 that indicates that there are in the physiological organism factors that tend to maintain the constancy of the internal environment (*58*). For instance, temperature, *p*H, or blood volume tend under physiological circumstances to maintain definite constancy. This view is essentially an extension of the concept evolved by Claude Bernard, namely, that there tends to exist a "milieu interne" in the body organization.

In a dynamic pathological process, such as that encountered in a local inflammation with the progress from an initial alkalinity to a frank acidity, there is the production by injured cells of a number of chemical factors. The common denominators liberated in the exudate seem responsible for the diversified biological manifestations of inflammation. Despite the changes in *p*H level at the site of an acute inflammation, there are produced various chemical factors having, nevertheless, the same biological properties—that is, regardless of whether a state of local alkalinity or local acidosis develops. In this way, a systemic homeostatic state is maintained throughout the duration of the inflammatory reaction (*50, 59*). The concept can be clarified further by listing the following examples.

1) Leukocytosis. In the initial alkaline stage of inflammation, the elevation in the number of circulating leukocytes is referable to the thermolabile leukocytosis-promoting factor (LPF). In the subsequent acid stage, the state of leukocytosis is ascribed to the liberation of the thermostable leukocytosis factor.

2) Leukopenia. In the alkaline phase of the inflammatory reaction, the liberation by injured cells of leukopenin seems to be the primary factor necessary to explain reasonably the occasional state of initial leukopenia, whereas in the acid stage the fall in circulating leukocytes is apparently due to the production of the leukopenic factor of acid exudates.

3) Permeability. The increased capillary permeability at the beginning of the inflammatory reaction is induced primarily by leukotaxine, whereas the increased seepage of fluid through the capillary wall in the acid stage seems to be referable to exudin.

4) Fever. Fever is primarily referable to the liberation of pyrexin. This substance is frequently although not invariably liberated in acid exudates. There is the possibility, however, that there is also a pyrogenic factor in polymorphonuclear leukocytes. This would possibly place this factor primarily in the initial or alkaline phase of the inflammatory reaction (*43–46, 60*).

In brief, it is by these various substances liberated at either an alkaline *p*H or at an acid *p*H, depending on the state of the inflammatory reaction at a given time, that the systemic manifestations are maintained in a constant state. In this manner, with a pathological process, physiological homeostasis of the organism as a whole is maintained despite the progressive local chemical changes in the area of acute inflammation.

## Repair

An inflammatory lesion heals. When damage is merely to the epithelial lining, normal regeneration occurs by simple mitosis. When a clean-cut wound is made at operation, relatively aseptically, and when the edges are brought together by suture, healing occurs rapidly by "primary union," or, as it is sometimes termed, "healing by first intention." There is hardly any fibrin or exudate. Fibroblasts move to the line of incision. At the line of cut a few polymorphonuclear leukocytes may appear because of the injury caused by the knife. Within a few days, firm union occurs. More and more fibroblasts and their collagenous bundles are deposited. The result is a scar or a cicatrice that becomes bloodless and usually persists indefinitely.

When the wound is open or if it suppurates, healing is somewhat slower and it proceeds somewhat as follows. Fibroblasts grow in abundance once the irritant has been localized and disposed by the various forces and by some of the factors discussed in this article. Accompanying their growth, there is active proliferation of the capillary endothelium. New capillaries sprout, growing from the base of the wound upward. When the scab of a wound, for instance, is removed there is a raw, reddish-appearing surface, rather granular. This is often referred to as "granulation tissue." The combination of the reparative factors consisting of fibroblasts and capillary sprouts with numerous new lymphatic channels is termed "vascular organization." After a longer period, more collagen is deposited. There is a tendency for contraction to occur, and we have, as a result, a scar or cicatrice.

This is a brief account of the well-known essentials in the repair processes of an inflamed area. Now, what is the stimulus that favors the growth of fibroblasts and capillary endothelium? A number of years ago it was found that exudative material recovered from an area of inflammation appears to contain one or perhaps even several growth-promoting factors (*61*). The experimental procedure consisted in repeatedly injecting into the tragal region of the rabbit's ear 0.5 milliliter of inflammatory exudate. The course of injections ranged from 1 to 7½ months. Following the cessation of injections, an interval of time ranging from 1 day to 7½ months was allowed to elapse. At that time, it was found that varying degrees of growth re-

actions appeared. These involved the cartilage and epithelium. The epithelial layer manifested pronounced hyperplastic response, with islets of keratinization. The dipping down of epithelial tonguelike projections into the corium was somewhat reminescent of the picture seen in some of the tar-induced cancer in rabbits described by the earlier writers. However, there was no definite evidence of any neoplastic formation. The architecture of the original cartilage plate was in many instances obliterated. Heterogenous, irregularly branching, and newly deposited cartilage cells were in evidence. In a few instances, metaplastic bone transformation appeared at the site of the original cartilage plate.

Recently it has been shown that the growth factor or factors present in exudates can be recovered as a diffusible component following vigorous dialysis, and subsequent concentration of the diffusate in a vacuum at reduced temperature of about 40° to 50°C. Such diffusible material induces proliferation without any significant inflammatory reaction (*52, 62, 63*). This can also be shown to some extent after repeated injections in the tragal region of the ears of rabbits (*12, 62*). A more convenient region is the vicinity of the nipples of nonpregnant rabbits. Hyperplasia of breast tissue and cystic dilatation of the ducts develop following the repeated local injections (*63*). Control injections with the diffusate of blood serum or saline injections fail generally to induce proliferative lesions to the same extent as found in the experimental areas. The nondiffusible material remaining in the cellophane tube can be extracted for necrosin and shown to be markedly injurious to cells. In brief, an injury factor can be dissociated from a a proliferative factor or factors liberated into the exudate at the site of inflammation (Fig. 5). These findings may be of significance in our further understanding of the reaction of repair following an acute inflammatory process. A picture may result which resembles that encountered in chronic cystic mastitis. Some workers have considered this type lesion to be precancerous in character (*64*). Furthermore, the process appears to be accelerated with the superimposition of a carcinogenic hydrocarbon—for example, methylcholanthrene (*12, 63*).

In a recent study on a homogenized aqueous extract of the ovaries of the sea urchin, *Arbacia punctulata*, an accelerator mitotic factor was observed that per se accelerates the cleavage of fertilized sea urchin ova (*12, 65*). In the same extract, a different fraction was also obtained that tends to be antimitotic in character and that actually retards cleavage (*12, 66*). The accelerator cleavage factor in the extract of the now-injured ovaries is diffusible. It is thermostable, and absorption spectrum measurements indicate that it probably is a nucleotide (*12, 65*). The diffusible proliferative factor of exudate described here appears, however, not to be a nucleic acid derivative. Preliminary chromatographic studies suggest the possibility that a peptide may be involved (*12*).

Finally, the presence of a growth-promoting factor liberated by injured cells may also prove to be of importance in our understanding of carcinogenesis or in the development of neoplastic processes in which cellular disequilibration seems to be brought about by a variety of means (for example, chronic irritation, virus infection, and hormone imbalance). When such cellular disturbance occurs and is superimposed on a genetically susceptible organism or in the presence of a chemical carcinogen, neoplastic development may be favored (*12, 42*).

## Conclusions

The presence of leukotaxine, exudin, the leukocytosis-promoting factors, necrosin, pyrexin, and the leukopenic factors in inflammatory exudates offers a reasonable explanation for the development of a fundamental pattern in inflammation. Observations suggest that an irritant, irrespective of its nature, severely injures cells, which in turn, as a result of their deranged metabolism, liberate these various common denominators. These chemical substances, which are to be regarded as constant products of marked cellular injury, are responsible for the recognized pattern of the inflammatory reaction.

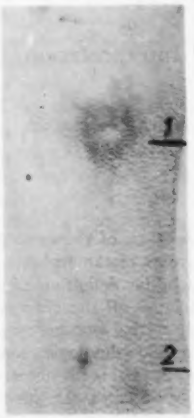


Fig. 5. The dissociation of the necrotizing factor in exudates (necrosin) from a present proliferative growth-promoting factor. (Area 1) The effect of necrosin extracted from the residual fraction of canine exudate after dialysis. Note the typical necrotizing inflammation. (Area 2) Note the absence of any pronounced visible effect when concentrated canine diffusate of an exudate was injected into the skin of a rabbit. [From V. Menkin, *Intern. Arch. Allergy and Appl. Immunol.* 4, 131 (1953)]

The interplay of the sequences described in this article (*67*) favors the localization and the ultimate disposal of the irritant. This leads to the final reparative phase of the injured area. Numerous observations indicate that repair may also be due to the liberation of a growth-promoting factor or factors by mildly injured cells. The growth-promoting factor or factors appear to be a diffusible component in exudative material. Necrosin seems to be released by the cell that is severely injured by an irritant, and thus the appearance of necrosin is significant in the development of the inflammatory process. Its chemical separation from the rest of the exudative fluid is a necessity in any endeavor to extract proliferative or reparative factors derived from probably less severely injured cells. Studies on invertebrate tissue (extract of ovaries of sea urchins) indicate the presence of a diffusible accelerator mitotic factor in the extract. This latter appears to be a nucleotide.

Sufficient material has been presented in the foregoing discussion to point out some of the important sequels of inflammation. For instance, it has been pointed out how the formation of glucose by injured cells complicates the all-important disease of diabetes. It has also been shown that the release of a toxic material, necrosin, from the area of inflammation may injure internal organs such as the liver and the kidneys. Pyrexin, which is liberated from injured cells at the site of an acute inflammation, is responsible at least in large part for the manifestation of systemic fever. It is thus clear that inflammation is not an exclusively localized reaction but that it may have far reaching effects on organs situated at a distance. Furthermore and conversely, as is pointed out here and elsewhere, various endocrine glands, such as the pituitary and the adrenal cortex, may exert definite influences on the course of the inflammatory reaction (*12*). The possible role of nerves is likewise not to be overlooked (*12*).

Finally, in the foregoing discussion, a biochemical theory of inflammation has been presented. There are, however, other biochemical aspects that can be described so that, necessarily, only a partial spectrum of the problem has been outlined here. A number of extremely important points have not been discussed for the reason that these aspects have either been very adequately treated previously and frequently by other investigators, or else they are not exactly relevant to the biochemical and immunological point of view of inflammation as I

have described it. Some of these have been treated elsewhere (*12*). For instance, the all-important subject of phagocytosis has intentionally been omitted here. Metchnikoff, the founder of the phagocytic theory, as well as his followers, have treated very adequately this paramount and well-known subject, now considered to be a cornerstone of inflammation.


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67. The investigations described in this article were supported in part by a grant from the U.S. Public Health Service and in part by a grant from the A. Wander, S.A., Berne, Switzerland. The material is primarily a summary of my own studies. Owing to space limitations, pertinent literature has had to be omitted from consideration. However, it has been quite adequately treated in my recent book. (*12*).


# Metamorphosis

## A Physiological Interpretation


Morris Rockstein


During the past decade there has been evident an increasing number of cooperative efforts by scientists who represent research disciplines considered widely separated. However, a few areas of the biological sciences remain in which the techniques of the physical scientist and experimental biologist are generally overlooked. Thus, taxonomists continue to depend on gross morphological or anatomical criteria for their deductions (*1*). In the few cases in which experimental or analytic data have been so employed (*2*), this use has been through the efforts of a few biochemists and physiologists who have applied their findings to phylogenetic or taxonomic deductions. I should like to show here how recent findings by other physiologists and myself may serve as a basis for the critical examination, if not the revision, of the established concepts of insect metamorphosis.

Although the definition of metamorphosis includes all the changes in form that occur during postembryonic development, most entomologists tend to limit their concept of this phenomenon to the transformation from the juvenile form (the larva) to the adult, or imago. One result of this limited concept has been artificial grouping of various orders of insects into groups such as the Ametabola, Paurometabola, or Holometabola according to the extent to which the juvenile stages differ in outward appearance from their corresponding imagoes. A number of competent entomologists admit that such a classification is artificial, especially from the phylogenetic standpoint. In his excellent monograph, Snodgrass (*3*) writes that "insects cannot be classified taxonomically according to the type of metamorphosis they undergo" and that "true metamorphic characters are adaptive structures . . . that have no phylogenetic counterpart in the adult evolution." This point is best illustrated by insects with complete metamorphosis, for they can hardly represent a monophyletic group. A more likely hypothesis is that holometaboly arose independently on several occasions during the evolution of the different orders of insects (*4*). In the course of his discussion, Snodgrass (*3*) also cites postemergence metamorphic changes, of which several cases are known, and anamorphosis or body segmentation after hatching. Since entomologists consider metamorphosis to be complete, except for sexual maturation, when the juvenile characters are discarded, the usual interpretation of these changes is that they are exceptions to the rule.

My own investigations and those of other physiologists interested in metabolic pathways in insects at different stages of development indicate a different interpretation. These findings suggest that visible transformation to the adult should not be considered as a terminal event but as one in a series of changes


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that result ultimately in the mature adult. If my interpretation is correct, a number of more cryptic biochemical changes must occur following the emergence of the adult. I shall call this series of changes "postemergence maturation" and characterize this period as one of "metachemogenesis."

## Patterns of Postemergence Maturation

Let me begin with a review of certain changes that I and others have observed in the adult forms of the worker honeybee, the housefly, and *Drosophila* sp. In my study of the cellular and biochemical changes that accompany the aging of the adult worker honeybee, I observed (*5*) that during the first week of adult life the cholinesterase activity of brain homogenates increased by 20 percent. In a subsequent investigation of the total body activity of the acid and alkaline glycerophosphatase system of adult worker bees, I found (*6*) that during the first week to 10 days of adulthood a reciprocal mechanism existed in which the activity of the acid enzyme rose by 90 percent, while that of the alkaline enzyme fell by about 50 percent.

In both studies, once the various levels of activity were reached, they remained constant through the remaining portion of the life of the bee. A study of the housefly, a species with a life span considerably shorter than that of the honeybee, reveals comparable data. Within 24 hours after the emergence of the adult, the brain cholinesterase activity may rise as much as 100 percent. This level is maintained for at least a week or longer (*7*). Studies of *Drosophila* have shown the occurrence of concomitant increments in wing-beat frequency and glycogen content during the first 7 days after adult appearance (*8*). Additional studies of *Drosophila* (*9*) have shown that both glycogen and fat accumulate rapidly during the first 2 days after adult appearance and then increase gradually to a maximum during the next 3 days. The maximum is maintained for at least 10 days.

In my interpretation, the changes in the worker honeybee, the housefly, and *Drosophila* represent fragments of integrated patterns of postemergence maturation at the cellular level. These changes are related to the final development of certain adult characters which in turn are related to various neuromotor activities, particularly those concerned with flying.

The enzyme cytochrome oxidase has been studied by investigators interested in the role of this enzyme and the entire cytochrome system in insect development. Obscured, if not hidden, in a number of reports there is repeated evidence that this system is also involved in postemergence maturation in a number of species of flies. In houseflies (*10*), its activity declines steadily during the first 2 days of pupal life and then rises sharply in a U-shaped curve resembling the oxygen consumption patterns of pupae of many holometabolous insects. Of particular interest is the fact that after adult emergence, the activity of this enzyme continues to rise, reaching a maximum by the third day of adult life, the value of which is 2 to 3 times that of an adult less than 1 hour old. In *Drosophila virilis* (*11*) a remarkably similar pattern is exhibited in the pupal and adult stages. The high level of activity of the late prepupal larva is reached again in the newly emerged adult. The enzyme continues to increase in concentration and reaches a maximum 3 days after emergence, the value of which is 80 percent above that of the young adult.

In a singularly well-planned study of certain moths, Carroll Williams and his coworkers have extended our understanding of the endocrine-enzymatic mechanisms that underlie and coordinate the differentiation, the growth, and the development of the adult from the pupal form. Thus, in the pupa of the cecropia moth, the onset of adult development is marked by the initiation of secretion of a growth and differentiation hormone by the prothoracic glands. This secretion has been triggered, in turn, by a stimulating hormone released from certain neurosecretory cells of the brain, as a result of exposure to low temperature. Concomitant with the burst of mitotic activity, signaling initiation of adult development, there occurs a rapid rise in cytochrome *c* synthesis. Conversely, during the early stages of adult development, the concentrations of cytochrome *b* and cytochrome oxidase, as well as the concentrations of two dehydrogenases, fall precipitously (*12*).

Of particular importance is the fact that rapid synthesis of cytochrome oxidase is begun on the second day of adult development. This marks a shift from a cyanide-insensitive system in the diapausing pupa, with a flavoprotein as the terminal oxidase, to a cytochrome system, the shift being essential to the metabolism of morphogenesis in the adult. It is not clear from Williams' reports, however, exactly how long the cytochrome system continues to play a dominant role in metamorphosis after the adult emerges. Evidence obtained in certain studies of *Drosophila virilis* (*11*) suggests that in insects such as the cecropia moth this dominance may also continue into the adult life.

This inference is strengthened by a recent study of the Japanese beetle (*13*), in which is reported a comparable pattern, from diapause through early adulthood, of changes in cytochrome oxidase activity. Despite certain differences between these findings and those for other species, a characteristic U-shaped activity curve during pupal "metamorphosis" is followed by an increase in cytochrome oxidase in the adult beetle, the maximum value of which is 2.5 times that of the highest activity observed in the last hours of pupal life. It is germane to these considerations to remark that in the early reports by Keilin of the occurrence of cytochrome compounds in animals (*14*), although generally unnoticed, the observation is to be found that the "cytochrome" concentration in insects rises during the early days of adult life.

## Sites of Action

The series of interrelated changes reflected in the obviously limited set of data summarized here must ultimately be defined more precisely at the tissue and cellular levels. Indeed, a few investigators have been engaged in describing the biochemical properties of the discrete cytoplasmic particles located in the flight muscles of certain orders of holometabolous insects (Diptera and Hymenoptera); these particles are the sarcosomes or giant mitochondria. In one species of fly, *Phormia regina*, the activity levels of cytochrome oxidase and catalase in isolated sarcosomes show a rapid drop during the first 4 days following adult emergence (*15*). More recently, as reported in a personal communication, Levenbook found that, during the first week of adult life in *P. regina*, not only the dry weight of the sarcosomes but also the concentration of cytochrome *c* triples in value. Moreover, other cytochrome components appear to rise proportionately during this same period. The concomitant rise in wing-beat frequency, reaching a maximum by the seventh day of adult life, points to the cytochrome system as playing an important role in the metabolism of wing action. At least in the case of this species of fly, a well-defined site of action of postemergence maturation, related to the full development of a particular adult function, appears to have been precisely located within the sarcosomes of the appropriate muscles.

The set of data I have cited emphasizes the continuity of the pupal and imaginal stages of holometabolous insects. As such, the data lend strong support to the theory of Poyarkoff, which interprets the pupa as a preliminary imaginal stage and not as the last nymphal instar, a theory for which Snodgrass (*3*) has ably presented a consid-

erable body of evidence of an embryological, comparative morphological, and endocrinological nature. In certain flying insects, this continuity has been markedly manifest in a well-integrated pattern of postemergence development of the neuromotor mechanism, reflected in the heightened activity of the cholinesterase system, in the enhanced storage of glycogen, and in the increased activity of enzymes concerned with respiration and energy release within the flight muscles. This period of cryptic metachemogenesis, through which the newly emerged adult must pass in order to complete its development, I consider to be, at the very least, a characteristic feature of holometabolous insects.

That a period of metachemogenesis may characterize all insects possessing *any* kind of metamorphic growth is suggested by other recent studies. In these studies (*16*), succinoxidase activity of the thoracic flight muscles in both sexes of the woodroach and in the male American cockroach, insects with gradual metamorphosis, has been observed to rise continuously after the final molt to a maximum by the tenth day of adult life. Moreover, Brooks (*17*) found that changes with age in succinoxidase activity in the basal leg and wing muscles of this insect are correlated with changes in color. In male cockroaches, for example, muscle color is white at the last nymphal molt and changes to pink shortly after emergence. The pink hue, as well as the enzyme activity, then increases rapidly in intensity and reaches a maximum at about 1 month after adult emergence. These findings for insects with gradual metamorphosis correspond closely to those presented earlier for holometabolous insects. They raise further doubts concerning the validity of the taxonomic separation of insects with metamorphic growth into three major categories, an otherwise arbitrary separation based on superficial criteria and with no great phylogenetic significance (*18*).

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# R. W. Marriott, Astronomer

Ross Walter Marriott was born in Paxton, Illinois, on 30 December 1882, and died at Hahnemann Hospital in Philadelphia on 19 October 1955. He entered the University of Indiana in 1902, obtained the bachelor's degree in 1906, and came to Swarthmore College that same year with the late John A. Miller, professor of mathematics and astronomy. Marriott received the master's degree at the University of Pennsylvania in 1911. He taught mathematics at Swarthmore College for 46 years, as an instructor (1907–10), assistant professor (1910–22), associate professor (1922–27), and professor of mathematics and astronomy (1927–52). He took an active part in making the adjustment of, and early observations with, the Sproul 24-inch refractor after it was installed at Swarthmore in 1911.

From 1923 to 1932 Marriott participated with Miller in the Swarthmore eclipse expeditions, and owing to his zeal and care Swarthmore College possesses a collection of fine coronal photographs. In the director's office of the Sproul Observatory hangs an oil painting of Miller and Marriott studying a solar eclipse photograph, painted by the late Owen D. Stephens, well-known artist of astronomical subjects.

Mariott was a perfectionist and was very critical of the results of his own observational efforts. He did not publish the measurements and discussions of some of his best plates, because he was not satisfied with the results.

The definition of Marriott's eclipse photographs is excellent; solar astronomers recognize the value of his large-scale photographs of the solar corona, which he generously shared, together with his unique knowledge about them. Outstanding are his large-scale photographs of the inner and outer corona at the time of the eclipse of 21 October 1930 at Niuafoou, Tonga ("Tin Can Island"), which are of exquisite quality and have been analyzed by several astronomers, particularly for the "jets," or small spicules.

The fruits of his long period of service in the teaching profession and his valuable collection of eclipse photographs remain as a monument to Ross W. Marriott of Swarthmore College.


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# News of Science

## International Cooperation in Arid Zone Research

Scientists who took part in the International Arid Lands Meetings in New Mexico last spring [*Science* **122**, 61 (1955)] will find many of the ideas that emerged there embodied in the broad program for international cooperation in arid zone research that UNESCO is planning to sponsor for the 2 years ahead. This became plain when outlines of that program were reviewed by the Advisory Committee on Arid Zone Research at its tenth session in November.

It is difficult to assess the results of an effort that aims at speeding up the flow of ideas across international and interdisciplinary boundaries, but in the 5 years that this UNESCO group has been operating there is substantial evidence of favorable effects. UNESCO has not sought to become an operating agency that would carry on its own research. Rather, it has been a kind of international catalytic agent—operating at modest cost—that has brought the experience of many individuals and groups to bear on problems common to the arid lands.

Although a popular account of this work recently has been published [*UNESCO Courier* **8–9** (1955)], it may be helpful to note three concrete examples of the kind of benefits that are flowing. (i) Under its fellowship scheme UNESCO enabled a young Peruvian scientist to study at the Salinity Laboratory in Riverside and to work with the Central Irrigation Board in India. He is now heading up a small research station on arid lands problems, Peru's first venture of this character. (ii) Under UNESCO's scheme for sponsoring international symposia, a number of scientists concerned with plant ecology gathered at Montpellier in 1953. [*Plant Ecology, Proceedings of the Montpellier Symposium* (1955)]. This has stimulated wider interest in the application of ecological knowledge to pasture management in the whole Mediterranean area, and Emberger has been invited to consult with workers in the field around the Eastern Mediterranean during the current spring. (iii) Several new research stations are taking shape in that area (government plans will probably be announced shortly), and increased work has been stimulated at established ones. No one knows precisely how far the UNESCO influence has extended, but it is clear that the net results already are solid.

In the years immediately ahead, it is expected that efforts will be channeled along the following lines, some of them noted in an earlier article [*Science* **120**, 15 (1954)].

1) Reviews of the status of research will be commissioned and published on four areas of investigation: (i) the history of land use, particularly agriculture, in arid and semiarid regions, which will try to emphasize the lines of study of past resources use, such as archeological studies of ancient water-spreading systems, that may throw new light on the potentialities and possible permanence of contemporary land use; (ii) the modification of soil structure under various land-use practices, such as grazing, dryland farming, and irrigation farming; (iii) the water requirements of plants, especially the efficiency of transpiration, the relationship of transpiration and photosynthesis, and the regulation of transpiration; (iv) methods of prospection and evaluation of water resources, study of the hydrological balance of aquifers, and methods for their recharge. In each case, a series of specific papers will be invited from workers in countries where there has been new research and then collated in a volume that will be given international distribution. Examples of papers of this character contributed by United States scientists in recent years are Howe's "Utilization of sea water" [*Reviews of Research on Problems of Utilization of Saline Water* (1954)], Hayward's "Plant growth under saline conditions" [*Reviews of Research on Problems of Utilization of Saline Water* (1954)], McGinnies' paper on plant ecology in the United States and Canada [*Plant Ecology—Reviews of Research* (1955)], and Linsley's "Report on the hydrological problems of the arid and semiarid areas of the United States and Canada" [*Reviews of Research on Arid-Zone Hydrology* (1953)]. The volume on saline water currently is being revised.

2) In cooperation with the Government of Australia an international symposium on climatology will be held in Australia in October 1956. There, an invited group numbering approximately 50 will give attention to current research and possible future lines of investigation relevant to arid and semiarid areas. The emphasis will be on microclimatology, and the program will include such topics as evaporation and the water balance, the thermal balance, interrelationships of climatic elements and flora and fauna, and modification of microclimate.

3) After extended exploration of the need for integrated surveys of associated resource problems in arid regions, the committee thought it best not to finance its own pilot surveys in selected countries. The complications of personnel, organization, and method seemed too strong. UNESCO will give financial help to countries that desire to develop survey groups in their own areas, it will offer fellowships to persons preparing for that work, and it will sponsor a review of the experience thus far by such groups as the Lands Research and Regional Survey of CSIRO in Australia, the watershed survey teams of the Department of Agriculture in the United States, and the desert agriculture surveys in Israel. This concern with integrated surveys is rooted in a desire to see new resources field work in the arid zones geared to contribute as effectively as possible to sound conclusions on resources development. Single-purpose surveys centering on one problem have been the rule often in the past, and for a variety of reasons they may prevail in the future, but where it may be practicable to combine basic study of landforms, climate, soils, vegetation, and hydrology in the same area at the same time this is to be desired.

4) A small program of research grants will be continued. This will favor projects that have probable international significance in areas where other financial support is available. Samples of projects that have received partial UNESCO subventions in recent years are Duvdevani's study of dew at the Earhart Laboratory and Schmidt-Nielson's study of the physiology of the camel at Beni-Abbes.

5) Major emphasis during the program proposed for 1957–58 is to be placed on the sector of the arid zone that lies between and includes Egypt and India. Aid to the research stations and fellowship grants to promising younger scientists will be concentrated in this area. Probably a special symposium will be held in this area. Here, in lands where great civilizations have flourished in delicate adjustment to scanty rainfall, there is heavy pressure of population on the land, and there is keen interest in new water-development undertakings. Pro-

motion of improved practices in the heavily grazed grasslands has been a major concern of the Food and Agriculture Organization in cooperation with the member countries through special working parties on pasture and fodder developments. FAO also has sought to direct constructive attention to the problems of drainage and salt accumulation in irrigated areas throughout the Middle East, problems that threaten the future stability of agriculture in large areas [FAO, *Report on Near East Regional Meeting on Irrigation and Drainage Practices* (1954)]. Success along these lines will require patient and knowing education aimed at applying present scientific knowledge of grazing and irrigated lands to local situations. Drastic readjustments in land use, land tenure, and community organization will be necessary in many instances. However, even with the most sensitive and effective educational work, there will remain major questions that will be solved only as a result of new research in the field. Thus, the UNESCO encouragement of basic investigations by well-trained staffs should lay the groundwork for extension and development activities a decade later.

In harmony with this effort to encourage some consistent government attention to basic research on problems of aridity in the zone between Cairo and New Delhi, the advisory committee has recommended early publication on an appropriately large scale of maps showing the water budget. Investigators of all aspects of arid lands have recognized the need for understanding water surplus or water deficit. These are covered in a project recently completed by Carter at the Laboratory of Climatology [D. B. Carter, "Climates of Africa and India according to Thornthwaite's 1948 classification," *Lab. Climatol. Publs.* **7**, 4 (1954)].

Financing of this UNESCO program beyond 1956 will depend on authorization from the general conference to be held next November. The arid zone work is listed as one of two "major projects" to be reviewed in the budget at that time. The tentative budget was examined by the executive board last November and now is before the member governments for consideration. At the meeting of the United States National Commission for UNESCO last autumn, there was extensive discussion of the arid zone activities, and there was some talk of organizing a national group or committee to deal with these activities. In a few countries, such as Mexico, this already has been done.

Any effort at international cooperation in encouraging research runs the risk of setting up top-heavy organization. There also is risk of loading the program so fully upon government agencies and, therefore, intergovernmental agreements that the easy, free movement of thought between individual scientific workers or scientific societies is impeded. So far UNESCO seems to have avoided these hazards, just as it has avoided becoming an operating agency on arid zone research. New ideas, fresh illumination, perfected techniques come from men working alone or in small groups. At best, an international organization can make it easier for them to communicate, a good deal easier to find official recognition and support, and much easier to move their findings into the arena of action.

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## New Marine Biological Laboratory in Brazil

A new marine biological laboratory, the Laboratorio de Biologia Marinha de São Sebastião, was inaugurated last September at the beach of Segredo, 6 kilometers south of São Sebastião, State of São Paulo, Brazil. The laboratory faces the channel between the continent and the mountainous island of São Sebastião. The first main building is equipped with electricity, gas, and tapwater, despite the fact that the whole laboratory is in close proximity to an almost untouched tropical forest on a small hill nearby. Another building was built as living quarters and mess hall for guest investigators and their families.

Segredo Beach borders a small bay limited at both ends by small rocky hills; the beach itself is covered with fine white sand. Being an almost untouched place, it still exhibits the tropical fauna and flora, marine as well as terrestrial, at their best. Its position is not far from the point where the island of São Sebastião southwards comes to an end; this makes available for the laboratory a great variety of biotopes: the channel, the open sea, and rocky and sandy beaches washed by calm as well as rough seas. The main building has a short access to the sea and was built approximately 4 meters from the maximum high tide.

The Laboratorio De Biologia Marinha de São Sebastião can be reached easily by ship (two weekly trips from Santos) or by car or bus (two daily trips, 6 hours from São Paulo). It is operated by a foundation (Fundação de Biologia Marinha), of which the University of São Paulo and its Departamento de Fisiologia Geral e Animal are founding members. It was built partially from grants made available by the University of São Paulo, the National Research Council of Brazil, and the Rockefeller Foundation. It is intended to be a place where Brazilians and foreigners who are interested in marine biology can find adequate means of research. Training courses for graduate students in biological sciences will be part of future laboratory activities. For more information write Prof. Paulo Sawaya, Caixa Postal 2926, São Paulo, Brazil.

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## AAAS Socio-Psychological Prize

Through the generosity of an anonymous donor, the AAAS offers an annual prize of $1000 for a meritorious essay in socio-psychological inquiry. The conditions of competition for the prize to be awarded at the 1956 annual meeting, New York, 26–31 Dec., are as follows.

1) The contribution should further the comprehension of the psychological-social-cultural behavior of human beings —the relationships of these hyphenated words being an essential part of the inquiry. Whether the contributor considers himself to be an anthropologist, a psychologist, a sociologist, or a member of some other group is unimportant as long as his essay deals with basic observation and construction in the area variously known as social process, group behavior, or interpersonal behavior. For ease of reference in the rest of this statement, this general area will be called "social behavior."

2) The prize is offered to encourage studies and analyses of social behavior based on explicitly stated assumptions or postulates, which lead to testable conclusions or deductions. In other words, it is a prize intended to encourage in social inquiry the development and application of dependable methodology analogous to the methods that have proved so fruitful in the natural sciences. This is not to state that the methods of any of the natural sciences are to be transferred without change to the study of social behavior, but rather that the development of a science of social behavior is fostered through observation guided by explicit postulates, which in turn are firmly grounded on prior observations. It may be taken for granted that such postulates will include a spatial-temporal framework for the inquiry. It may properly be added that the essay should foster liberation from philosophic-academic conventions and from dogmatic boundaries between different disciplines.

3) Hitherto unpublished manuscripts are eligible, as are manuscripts that have been published since 1 Jan. 1955. Entries may be of any length, but each should present a completed analysis of a problem, the relevant data, and an interpretation of the data in terms of the postulates with which the study began.

Preference will be given to manuscripts not over 50,000 words in length. Entries may be submitted by the author himself or by another person on his behalf. Each entry should be accompanied by four copies of an abstract not to exceed 1200 words in length.

4) Entries will be judged by a committee of three persons considered well qualified to judge material in this field. The judges will be selected by a management committee consisting of the chairman and the secretary of Section K and the executive officer of AAAS. The committee of judges reserves the right to withhold the prize if no worthy essay is submitted.

5) Entries should be sent to Dael Wolfle, Executive Officer, American Association for the Advancement of Science, 1515 Massachusetts Avenue, NW, Washington 5, D.C. Entries should be submitted in quadruplicate. The name of the author should not appear anywhere on the entry itself but should be enclosed on a separate sheet of paper which also gives the author's address and the title of his essay. To be eligible for consideration for the prize that will be awarded at the 1956 annual meeting of the Association, entries must be received *not later than 1 Sept. 1956.*

## Mammary Carcinomas in Mice

Alfred Taylor and Roger J. Williams have reported [*Proc. Natl. Acad. Sci. U.S.* **42**, 54 (1956)] a method of control of C3H mouse mammary carcinoma when grown in the yolk sacs of developing chick eggs. They pointed out that a specific tumor grown under these conditions would not be expected to behave in the same way in its normal host and that any success in controlling cancerous growth in their experiments could not be carried over unchanged to the control of cancer in man.

In one control series of eggs inoculated with mouse tumors, 57 out of 58 of the embryos were dead by the sixteenth day of incubation; the one remaining alive bore a large tumor. In a parallel experimental series, treated as described in a subsequent paragraph, out of 140 similarly inoculated eggs, 86 remained alive on the sixteenth day. Of these, 81 contained traces of what may have been viable tumor tissue and five showed no observable tumor tissue. The effect of the treatment had been to reduce the tumor growth, which in untreated eggs is fairly uniform. Tumors in untreated developing chick egg yolk sacs grow rapidly; for example, they double in size from the eleventh to twelfth day of incubation.

The treatment consisted in the combination of an elevated temperature of incubation (40°C instead of the usual 37.2°C), which had previously been found to be effective in slowing tumor growth, and the application of chemicals that by themselves showed some inhibitory effect. The chemicals used were aminopterin (4-aminopteroylglutamic acid) and triethylenemelamine. In a series in which the former compound was used, tumor growth for a 24-hour period at 37.2°C was 62 percent as great as it was in the control eggs; at 40°C in the same experiment, the tumors decreased in size during the test period.

Triethylenemelamine was more effective. In similar experiments, the tumors in treated eggs at 37.2°C averaged only 19 percent as large as those of the controls; those at 40°C either failed to grow or regressed in size.—G. DuS.

## News Briefs

■ The design and development by Argonne National Laboratory of a multi-billion-volt particle accelerator to be built at its DuPage County site has been authorized by the U.S. Atomic Energy Commission. The Argonne machine, based on a design conceived by the laboratory's staff of scientists, will greatly ease the usual problems of construction. It will permit the rapid attainment at reasonable cost of an energy greatly in excess of that of any machine now in operation.

■ The Salk vaccine is helping win the battle against poliomyelitis in Canada, reported Martin, the Minister of National Health and Welfare, in a reply tabled last month in the House of Commons. He said:

"The use of the Salk vaccine in Canada during 1955 was the most ambitious mass immunization program ever undertaken in this country. It also provided an opportunity for carrying out a nationwide epidemiological study, the results of which have demonstrated the safety and effectiveness of the vaccine as an immunizing agent. In addition, the whole program offered an outstanding example of cooperation between federal, provincial, and local health authorities and served to bring home to the people of Canada in dramatic fashion the value of public health activities generally."

■ Approval of the sale of 129 tons of heavy water to six nations for assistance in their peacetime applications of atomic energy has been announced by the U.S. Atomic Energy Commission. Sixteen tons of the material have been shipped abroad.

The initial consignments of 11 tons to Great Britain and 5 to France were manufactured at the commission's plant at Dana, Ind. Heavy water also is produced at its facilities in South Carolina. All sales are at the price of $28 per pound announced 8 Aug. 1955.

The total amounts (in tons) approved for sale are as follows: United Kingdom, 50; France, 30; India, 21; Australia, 11; Italy, 10, and Switzerland, up to 7, with 2 tons to be delivered by August 1957.

## Scientists in the News

The Kimber Genetics medal of the National Academy of Sciences for 1956 will be presented to SEWALL WRIGHT, professor of genetics at the University of Wisconsin, during the annual meeting of the academy, 23–25 Apr. 1956. Wright has made important contributions in both theoretical and experimental genetics.

The Kimber Genetics award of the academy was established in 1954 by the Kimber Farms Foundation to provide recognition of great achievement in the science of genetics. In selecting recipients for the Kimber award, the academy has the cooperation of the American Association for the Advancement of Science and the Genetics Society of America.

JOHN R. HANSBROUGH of the Northeastern Forest Experiment Station has been named chief of the Division of Forest Disease Research at Washington, D.C., the U.S. Forest Service announced. He succeeds Lee M. Hutchins, who retired 31 Dec. 1955.

WILLARD F. LIBBY, Commissioner of the U.S. Atomic Energy Commission, will be presented with the medal for scientific achievement of the City College of New York Chemistry Alumni Association on 27 April. Libby will deliver the association's eighth bicentennial science lecture on "Peaceful uses of atomic energy."

LOUIS PILLEMER, professor of biochemistry at Western Reserve University, delivered the fifth R. E. Dyer lecture at the National Institutes of Health. He spoke on "The properdin system." Pillemer and his colleagues identified a new blood protein, properdin or "the destroyer," in natural immunity that may prove to be important in radiation sickness, shock, and experimental infections.

BEN PECKHAM, faculty member at the Northwestern University Medical School, will become professor and chairman of the department of obstetrics and gynecology at the University of Wisconsin Medical School on 1 May.

VICTOR HAMBURGER, professor of zoology at Washington University, St. Louis, gave the Mellon lecture for the Society of Biological Research at the University of Pittsburgh School of Medicine on 16 March. His subject was "The life history of a nerve cell."

RALPH BOWN, a vice president of the Bell Telephone Laboratories, retired on 1 Mar. after 37 years of service. For the past year he has been vice president in charge of patent activities and of long-range planning of laboratories programs. Previously he had been vice president in charge of research.

Bown has been honored by numerous professional societies and by the Government. In 1955 he was appointed chairman of the U.S. Patent Office Advisory Committee. He is also chairman of a technical advisory committee on electricity and electronics for the National Bureau of Standards, and a member of the Army Scientific Advisory Panel.

Bown, who has been a pioneer in communications engineering, was awarded the 1926 Morris Liebmann memorial prize by the Institute of Radio Engineers for his research in wave transmission phenomena. He served as president of the IRE in 1927, and in 1949 received the institute's annual medal of honor for his leadership in institute affairs and for his extensive contributions to the field of radio.

Much of Bown's technical work has been concerned with various aspects of radio broadcasting, and overseas telephony and microwave radio relay systems. He directed the New York-Boston radio relay project, opened for experimental service in November 1947, which was the first link in the transcontinental radio relay system.

A native of Fairport, N.Y., Bown received the degrees of mechanical engineer, master of mechanical engineering, and doctor of philosophy from Cornell University. After serving as a captain in the Signal Corps during World War I, he began his telephone career in 1919 with the development and research department of the American Telephone and Telegraph Company. There he specialized in various aspects of radio broadcasting and in ship-to-shore and overseas telephony.

In 1934 he was appointed assistant director of radio research at Bell Laboratories; in 1936, director of radio and television research; in 1944, assistant director of research; in 1946, director of research; and in 1951, vice president–research.

During World War II Bown served with the National Defense Research Committee, specializing in radar, and in 1941 he visited England to study operations under combat conditions. He also served as a consultant to the Secretary of War. After his retirement Bown will be associated with the N.W. Ayer and Son advertising agency as a consultant in public relations in the field of science.

The recently organized Chemical Warfare Laboratories of the Army's Chemical Corps at the Army Chemical Center, Md., has announced the following appointments:

DONALD H. HALE has been placed in command of the laboratories. He received his doctorate in physics from the University of California and was formerly deputy commander of the Chemical Corps Research and Engineering Command.

L. WILSON GREENE, who formerly was technical director of the Chemical and Radiological Laboratories at the Army Chemical Center, has been appointed chief technical adviser to the Chemical Corps.

SEYMOUR P. SILVER has been appointed deputy for scientific activities. He has been associated with the Chemical Corps since 1938, and has served as consultant to civilian health organizations in air pollution problems.

The laboratories are divided into four directorates. WILLIAM H. SUMMERSON has been appointed director of research; ALBERT R. DREISBACH, director of medical research; DONALD E. YANKA, director of development, and JAMES P. MITCHELL, director of technical services.

LEONARD G. GINGER has been promoted to director of chemical research in the research and development division of Baxter Laboratories, Inc.

LEONARD REIFFEL has been appointed manager of the physics research department of Armour Research Foundation at Illinois Institute of Technology. He will direct research in acoustic design, sound and vibration control, nuclear physics, light and optics, physics of solids, and magnetics.

ALFRED C. REDFIELD, senior oceanographer at the Woods Hole Oceanographic Institution and professor of physiology at Harvard University, and LAURENCE IRVING, biologist at the U.S. Public Health Service's Arctic Health Center, Anchorage, Alaska, and professor of biology at Swarthmore College, Pa., were among 12 scientists who received the honorary degree of doctor of philosophy at the graduation ceremony of the University of Oslo, Norway.

JACOB E. JANSEN, who has been with the B. F. Goodrich Company since 1938, has been named director of organic chemicals research in the company's Research Center, Brecksville, Ohio.

U. PENTTI KOKKO has joined the staff of the U.S. Public Health Service's Communicable Disease Center at Atlanta, Ga., as assistant chief of the center's laboratory branch. Prior to coming to Atlanta, Kokko was director of the division of local health services of the Kentucky State Department of Health.

A. J. HAAGEN-SMIT, professor of bio-organic chemistry at California Institute of Technology, has been appointed to head the air pollution control research program of Southern California Edison Company.

## Recent Deaths

FRANCIS BLOSSOM, New York, N.Y.; 80; engineer; former special consultant to the War Department; 12 Mar.

ARTHUR L. DUBUSC, Elizabeth, N.J.; 90; pioneer submarine builder; 9 Mar.

PAUL J. KOLACHOV, Bogota, Colombia; 56; chemurgy expert; director of Colombia's Department of Technological Investigation; 29 Feb.

FRANK J. O'BRIEN, White Plains, N.Y.; 65; child psychiatrist; 13 Mar.

WILLIAM ROBERTSON, Philadelphia, Pa.; 85; professor emeritus at Temple University Medical School; 9 Mar.

OTTO ROSENDAHL, Minneapolis, Minn.; 80; emeritus professor of botany and former chairman of the department at the University of Minnesota; 4 Mar.

WALDO SHUMWAY, Hoboken, N.J.; 64; zoologist; provost of Stevens Institute of Technology; 8 Mar.

LUKAS TINBERGEN, Groningen, Netherlands; 39; professor on the faculty of sciences at the University of Groningen; 1 Sept. 1955.

## Education

■ The fourth annual Workshop for College Professors will be offered at the University of Michigan, 25 June–13 July. Further information may be obtained from Algo D. Henderson, Director, 242 U.E.S., University of Michigan, Ann Arbor.

■ Some 1000 Washington area scientists and engineers took over the classes of approximately 100 junior and senior high schools for 2 days, 15 and 16 Mar., leaving 400 regular teachers free to attend the convention of the National Science Teachers Association, and giving

the local scientists a chance to discuss their work with students. The project, sponsored by the Washington Academy of Sciences and the D.C. Council of Engineering and Architectural Societies, was led by the Joint Board on Science Education for the Greater Washington Area. The D.C. Science Supervisors helped secure the substitute teachers, while Science Service gave the program financial support.

■ The nation's network of educational television stations maintained by the Educational Television and Radio Center, Ann Arbor, Mich., will present this fall a series of ten programs featuring Glenn T. Seaborg of the University of California. The series, now being filmed on the California campus by the San Francisco station for the center, is called *The Elements*. It will explain the various natural and synthetic elements and show the importance of chemistry in the life of a typical American family.

## Grants, Fellowships, and Awards

■ Aided by a grant of $23,000 from the National Science Foundation for the 3-year period 1956–58, the entomology department of the Bishop Museum, Honolulu, is beginning a program on the zoogeography of Pacific insects. Emphasis at the start will be on field work in the assumed source areas of the oceanic Pacific insect fauna—the island groups from the New Hebrides to Southeast Asia, particularly New Guinea. Under the supervision of J. L. Gressitt, arrangements are being made for several entomologists to participate in the field work, and collaboration with other organizations interested in the area is anticipated. It is expected that research on the collections may be carried on largely by the specialists collaborating with the Bishop Museum in the *Insects of Micronesia* series, of which nine issues have been published to date.

■ The Atlas Powder Company, manufacturer of explosives, chemicals, and activated carbons, will award eight $1000 college scholarships again this year. The grants will go to students who will be seniors during the 1956–57 college year who are majoring in chemistry or any branch of engineering. Thirty-eight colleges and universities have been invited to participate in the program. Scholarships will be awarded on the basis of scholastic records and the recommendations of faculty members who are acquainted with the applicants. Extracurricular activities and financial need will also be factors. Winners of the awards will be announced 15 May. Successful candidates also will have a chance to gain practical experience by paid summer work with Atlas between their junior and senior years. However, successful candidates will not be obligated to work for Atlas either during the summer or after graduation, nor will Atlas assume any commitment to employ the student.

■ The Foundations' Fund for Research in Psychiatry, New Haven, Conn., awarded 13 grants during 1954–55. Of these, ten grants were made in behalf of new research programs or of programs that had not previously received the foundation's support. Of these ten grants, one was for a period of 1 year, two were for 2 years, and the remaining 7 were for 3 years.

The total amount expended for all 13 grants was $212,955.50, and commitments for the years 1955–56 and 1956–57 are in the combined amount of $262,513.87.

The directors of FFRP consider that research in all branches of the behavioral and biological sciences is needed if an integrated scientific basis for the field of psychiatry is to be developed. There exists, however, an especially urgent need for investigations on the level of clinical psychiatry, including psychoanalysis. These latter fields have heretofore provided important new ideas and have also brought to light important new phenomena, thus posing significant research problems. This foundation is especially interested in supporting research that will bring scientific rigor and ingenuity of method to the facts and problems which most directly confront the psychiatrist.

## Miscellaneous

■ The manner in which the mining of nonferrous minerals may stimulate other economic activities in underdeveloped countries and thus contribute to their development is the subject of an economic report that has been published recently by the United Nations. The 129-page study, entitled *Non-Ferrous Metals in Underdeveloped Countries* is the latest in a series initiated by the secretary-general following the 1949 Scientific Conference on the Conservation and Utilization of Resources that was sponsored by the U.N.

Apart from the major nonferrous metals—copper, lead, zinc, tin, and aluminum—some of the minor ones that are used chiefly for iron and steel alloys, such as colombium, vanadium, molybdenum, tungsten, chromium, nickel, and cobalt are also considered. The report contains five maps showing the locality of mines and smelters of major nonferrous metals in underdeveloped countries.

■ A group of engineers at the Marquardt Aircraft Company has inaugurated an experimental unit of "Science scouts" in cooperation with the San Fernando Valley Council of the Boy Scouts of America.

The unit, known as Marquardt Science Scouts Post, has scheduled assignments covering the launching of a hypothetical spaceship, the use of solar and nuclear energy, and an examination of the social implications of scientific progress.

■ The Association for Applied Solar Energy will publish the first issue of a new journal, *The Sun at Work*, in April. Information about the journal may be obtained from the Editor, Suite 204, Mayer-Heard Building, Phoenix, Ariz.

■ The Atomic Energy Commission has announced that it has adopted a policy of booking its traveling exhibits on peacetime applications of atomic energy to qualified exhibitors free of transportation costs and rental charges. The commission for some years has maintained a relatively small number of atomic energy exhibit materials that have been made available to exhibitors on a daily rental fee basis, with each exhibitor defraying transportation charges as well as costs of presentation. Under the new policy, the exhibits will be available to qualified exhibitors free of transportation costs and rental charges; however all other expenses relative to showings will continue to be borne by the exhibitors.

The exhibits now in circulation are soon to be replaced by new units. Details regarding AEC exhibit materials that are available, as well as information on those being planned, may be obtained from the American Museum of Atomic Energy, Oak Ridge, Tenn. The new exhibits probably will be completed and available for showings starting about 15 June. Requests for bookings will be accepted by the museum on and after 1 Apr.

■ Henri Poincaré's striking predictions of more than a half-century ago on the developments in physics are available for comparison with what has actually happened in "Principles of mathematical physics," which appears in the April issue of *The Scientific Monthly*. Other articles included are "Role of science in marine fisheries: limitations and potentialities," R. E. Coker; "Atmospheric pollution and zoning in an urban area," François N. Frenkiel; and "Radar echoes from birds and insects," Lewis L. Bonham and Lamont V. Blake. Readers' comments on the Julian Day calendar, "Form and symmetry in organisms," and crop yield data are given in the "Letters" section. Twelve books are reviewed.

# Reports and Letters

## Correlation of Major Vegetation Climaxes with Soil Characteristics in the Sonoran Desert

Soil characteristics determined from samples taken over a 14-mile transect of desert vegetation in southern Arizona have yielded highly significant differences associated with two distinctly different climax vegetation types. The transect is in the Basin and Range Physiographic Province of the inland Southwest and is over alluvial land, a soil taxonomic unit that in this case refers to the unconsolidated alluvium of a desert climate. This type of alluvium, known as fanglomerate, characterizes most of the soils of the Sonoran Desert.

The transect is located on the western slope of the Tucson Mountains, a low desert range west of Tucson, and the adjacent Avra Valley, from approximately 3400- to 2000-feet elevation. The soil samples analyzed were taken to a depth of 3 feet from 16 soil-sample stations along the transect. Since this type of desert alluvium is generally deep and shows little or no profile development, samples were arbitrarily drawn at 6-inch intervals to indicate any specific soil property to a much greater depth than 3 feet.

The lighter and more rocky soil of the higher slopes supports the relatively complex Paloverde-Sahuaro (*Cercidium-Cereus, 1*) vegetation type, whereas the finer soil of the lower slopes and valley supports the relatively simple Creosotebush-Bur Sage (*Larrea-Franseria, 1*) association. These are the two major climax vegetation types of the Sonoran Desert in Arizona, the Paloverde-Sahuaro association constituting a distinct *tree* climax and the Creosotebush-Bur Sage association forming a characteristic *shrub* climax. The *same* macroclimate exists for both climax vegetation types.

A broad ecotone extends along the lower western slope of the Tucson Mountains and the adjacent Avra Valley, varying locally in elevation from approximately 2800 to 2200 feet. The difference in slope of less than 4 degrees between the upper portion of the transect and its lower end is insufficient, as is the elevational difference, to constitute a causal factor in the given vegetational difference.

Standard determinations were made for soil texture (mechanical analysis), moisture equivalent, moisture content, capillary rise, dispersion rate, and salinity. Wilting coefficients were determined by the indirect method of Briggs and Shantz (*2*), inasmuch as the soil samples are variants within a closely related soil group. Results are given in Table 1 for moisture equivalent, wilting coefficient, and moisture content. It is observed that highly significant differences obtain for soil characteristics associated with the two different major vegetation types.

The differences between these soils in pertinent physical and physiological characteristics, such as moisture equivalent and wilting coefficient, are attributable to the significant difference in the texture of these soils. Available soil moisture during the critical dry seasons determines the occurrence of one vegetation type over the other. This is best expressed by the wilting coefficient. The less colloidal, more sandy, and more rocky soil supporting the *Cercidium-Cereus* association has a wilting coefficient of approximately one-half that of the finer soil of the *Larrea-Franseria* association, whereas the values in moisture equivalent and moisture content for the latter are twice those of the former. This means that with a value of 50 percent less total soil moisture, twice the amount of soil moisture is available for plant use in the Paloverde-Sahuaro association than is available in the Creosotebush-Bur Sage association. Intermediate values in these and other soil properties obtain for the broad area of ecotone where one distinct vegetation type first merges and then gives way to the other.

In summary, from analysis of pertinent soil characteristics and their correlation with climax vegetation types of the Sonoran Desert, it is concluded that here specifically different soil attributes characterize, and are intimately associated with, distinctly different and major climax vegetation types existing under the same macroclimate.

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Table 1. Statistical comparison of soil characteristics of the two major climax vegetation types of the Sonoran Desert in Arizona.

| Soil characteristic | N | *Larrea-Franseria* | N | *Cercidium-Cereus* | *t* | *P* |
|---|---|---|---|---|---|---|
| Moisture equivalent (%) | 24 | 12.2 ± 0.61 | 24 | 6.6 ± 0.14 | 8.9 | < .001 |
| Wilting coefficient (%) | 24 | 6.6 ± 0.33 | 24 | 3.6 ± 0.08 | 8.8 | < .001 |
| Moisture content* (%) | | | | | | |
| Wet (approx. field capacity), summer rainfall season, July | 12 | 9.1 ± 0.90 | 12 | 5.5 ± 0.16 | 7.3 | < .001 |
| Dry, postsummer rainfall season, December | 12 | 3.4 ± 0.41 | 12 | 1.4 ± 0.09 | 4.6 | < .001 |

* Moisture content here refers to the amount of water present in a given soil at a given time determined on the basis of a percentage of the oven-dry weight of a given sample at 105°C. For valid comparative purposes, samples were taken simultaneously at different soil stations.

**References and Notes**

1. *Cercidium microphyllum-Cereus gigantea* and *Larrea tridentata-Franseria dumosa*, respectively.
2. L. J. Briggs and H. L. Shantz, *Bot. Gazette* 53, 25 (1912).

16 September 1955

## Detection of Sex of Fetuses by the Incidence of Sex Chromatin Body in Nuclei of Cells in Amniotic Fluid

Identification of genetic sex on the basis of the incidence of the sex chromatin body observed in the nuclei of oral mucosa smears has recently been described (*1*). The technical concept appears to be directly applicable to the cellular debris in amniotic fluid. Since all such cells are of fetal origin, and since the sex chromatin body incidence is independent of the hormonal milieu (*1, 2*), it should be possible, therefore, to establish the genetic sex of the fetus *in utero* by this method. This has been done.

Amniotic fluid has been obtained from pregnant women by direct aspiration of the amniotic sac with a needle and syringe. This fluid is centrifuged, and the sediment is spread on a slide treated with egg albumen. The slide is immersed at once in equal parts of 95-percent ethyl alcohol and ethyl ether for 2 to 24 hours. The fixed smears are passed through 70-percent and 50-percent ethyl alcohol

and distilled water for 5 minutes each. They are then stained for 8 minutes in 1-percent cresyl echt violet (*3*) (British Drug House) and are differentiated in 95-percent ethyl alcohol for 3 to 5 seconds. The stained smears are rinsed in absolute ethyl alcohol until nuclear detail is clear on examination under the high dry objective of the microscope. They are then mounted in Permount.

The mounted smears are studied under the oil-immersion objective of the microscope. The sex of the newborn infant has been established on the basis of external physical examination.

Many of the nuclei in amniotic fluid debris are not suitable for identification of the sex chromatin body. Some are markedly pyknotic, while other take the stain poorly or are badly fragmented. White blood cells may also appear in the fluid obtained from patients in labor.

The incidences stated in Table 1 are based only on examination of well-stained healthy nuclei that are assumed to be desquamated from the amnion, skin, or mucosae of the fetus. Such a nucleus with a sex chromatin body is shown in Fig. 1.

Observer 1 counted 100 nuclei in each instance. Observer 2, who studied some of the smears counted by observer 1, counted 50 nuclei. Neither observer knew the sex of the infant or the other observer's results at the time the counting was done.

It will be noted that there is no overlap between the maximum counts on male fetuses and the minimum on females. The means are separated by a gap 4 to 5 times the mean for male fetuses; and the extremes, by a gap 2 to 3 times the male fetus mean. Since there are no erroneous identifications of anatomic sex in the group, these observations are overwhelmingly significant.

The amniotic fluid was obtained at or near full term, with the exception of one instance of fetal death *in utero* of unknown etiology at 32 weeks. The incidence of nuclear pyknosis was increased in this case, but a sufficient number of satisfactorily stained nuclei were found nevertheless.

One smear not included in Table 1 requires comment. It was prepared from amniotic fluid obtained at cesarean section in a patient who was fully dilated with ruptured membranes and a fecal fistula in the vaginal vault. The fluid was grossly contaminated with maternal feces. The smear includes many polymorphonuclear leukocytes and unstained digested vegetable matter. It was originally counted by observer 1 as having 54 percent of nuclei with the sex chromatin body and later by observer 2 as 22 percent. A third observer found a count of 20 percent. The fetus was a male. The count by observer 1 was made at 2 A.M.

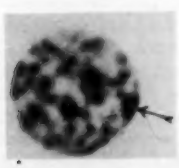

Fig. 1. Nucleus of a cell in a stained smear of amniotic fluid debris (×3300). The arrow points to the sex chromatin body along the nuclear membrane.

Table 1. Incidence of sex chromatin body in amniotic fluid cell nuclei.

| | *Observer 1* | | | *Observer 2* | | |
|---|---|---|---|---|---|---|
| | No. | Range (%) | Mean (%) | No. | Range (%) | Mean (%) |
| Males | 14 | 6–17 | 10 | 6 | 6–22 | 13 |
| Females | 16 | 49–71 | 59 | 6 | 42–70 | 54 |

Decisions on which nucleus to count and which to ignore in these amniotic fluid smears will vary from time to time, from observer to observer, and will depend in part on the quality of the stained smear and the density of the cell populations. In the present study, frequent consultation between observers on the appearance of individual nuclei served to limit the range of these variables, but the operation of chance produced some variation between two counts on the same smear (*4*). It is, therefore, not to be expected that repetition of these observations by others will produce results of an identical order of magnitude. The counts obtained on oral mucosa by Marberger *et al.* have lower means but the same wide separation between the means without overlap (*1*). The likelihood of finding a count on a genetic male that even approaches the lowest count on a genetic female is virtually nil by either method, provided that the absolute size of the counts is determined by conditions held constant for any group of counts made.

That the smears must be obtained and read for this purpose under ideal conditions is emphasized by the exceptional case cited in a foregoing paragraph. The unusual amount of debris of maternal origin in this amniotic fluid with a fecal fistula and late labor with ruptured membranes resulted in a smear that was misread by a fatigued observer.

It has been assumed that the infants identified as female after birth do not include any instances of gonadal agenesis who might be genetic males.

The techniques of exfoliative cytology have been applied to the determination of genetic sex of the fetus *in utero* by the incidence of the sex chromatin body in the cellular debris of amniotic fluid.

The mean incidence of this body in the nuclei found in the fluid of female fetuses is several times that found in male fetuses, and the minimum incidence in females in this series is approximately twice the maximum incidence among male fetuses. There are no erroneous determinations. This result is highly significant.

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### References and Notes

1. E. Marberger, R. A. Boccabella, W. O. Nelson, *Proc. Soc. Exptl. Biol. Med.* **89**, 488 (1955).
2. M. L. Barr, *Anat. Record* 121, 387 (1955); K. L. Moore, M. A. Graham, M. L. Barr, *Surgery Gynecol. Obstet.* **96**, 641 (1953); *Anat. Record* 121, 422 (1955).
3. M. L. Barr and E. G. Bertram, *Nature* **163**, 676 (1949).
4. E. G. Bertram, instructor in anatomy at Marquette University School of Medicine, provided valuable advice in the technique of staining these smears.

28 December 1955

## Reagent for Differentiation of 1,4- and 1,6-Linked Glucosaccharides

Buchan and Savage have employed a mixture of aniline, diphenylamine, and phosphoric acid as a spray reagent for the detection and estimation of sugars on paper chromatograms (*1*). In applying this reagent to characterize the end products of enzymic degradation of starchlike substrates, we have observed variations in the color of oligosaccharide spots on paper chromatograms. Further investigation with known 1,4- and 1,6-linked glucosaccharides (*2*) revealed that these differences correlated to a certain extent with variations in the structure of these compounds.

Those saccharides in which the carbon-4 hydroxyl proximal to the reducing end of the molecule was combined in glucosyl linkage yielded blue to purple colors, whereas those saccharides in which this hydroxyl was uncombined yielded slate, green, or yellow spots, depending on the concentration of the substance per unit area of the paper chromatogram (Table 1). Aso and Yamauchi (*3*) have recently observed independently that the color of the reaction products of other

Table 1. Color and spectral characteristics of amine-sugar reaction product. The absorption peak for maltose in the α region was taken as unity. (X), (S), and (I) refer to the maximum, shoulder, and minimum, respectively, in the indicated spectral region; (A) indicates absence of characteristic.

| Saccharide | Color | | Relative molar absorbency in spectral regions | | | | Ratio α/δ |
|---|---|---|---|---|---|---|---|
| | Concd. | Dilute | α | β | γ | δ | |
| Maltose 1,4- | Blue | Purple | 1.00(X) | 0.75(S) | 0.62(X) | 0.51(I) | 2.0 |
| Maltotriose 1,4- + 1,4- | Purple | Purple | 0.74(X) | 0.63(S) | 0.29(A) | 0.27(I) | 2.8 |
| Panose 1,6- + 1,4- | Blue-black | Purple-brown | 1.11(X) | 0.90(X) | 0.63(S) | 0.52(I) | 2.1 |
| Isomaltose 1,6- | Slate | Green | 0.48(X) | 0.41(X) | 0.37(I) | 0.83(A) | 1.2 |
| Isomaltotriose 1,6- + 1,6- | Slate-brown | Green | 0.46(X) | 0.44(X) | 0.37(I) | 0.39(A) | 1.3 |
| Glucose | Slate | Green-brown | 0.53(X) | 0.50(X) | 0.49(S) | 0.49(S) | 1.1 |

aniline sprays with a series of glucobioses was characteristic of the linkages between the bioses but independent of their anomeric configurations.

These qualitative observations also confirm and extend the findings of Giri *et al.* (*4*), who noted similar colors for glucose, maltose, and isomaltose with the Buchan-Savage mixture as a brush reagent.

In addition to the compounds listed in Table 1, confirmatory evidence for this color distinction was obtained from the reaction on paper chromatograms of a mixture of oligosaccharides of the maltose series and a corresponding mixture of the isomaltose series from bioses to octaoses.

Figure 1 illustrates some typical spectra obtained by placing a slip of reagent-treated paper containing the sugar spots in the path of light from a Beckman D.U. spectrophotometer. A summary of the spectral characteristics shown in Table 1 shows the presence of four spectral regions. All compounds tested showed an absorption peak in the α (610 to 640 mμ) and β (520 to 540 mμ) regions, except for the presence of a shoulder for maltose in the β region. The relative molar absorbencies of the maltose series and of panose were considerably higher in these regions than the corresponding absorbencies of glucose and the isomaltose series, whereas this difference was much less in the blue end of the spectrum.

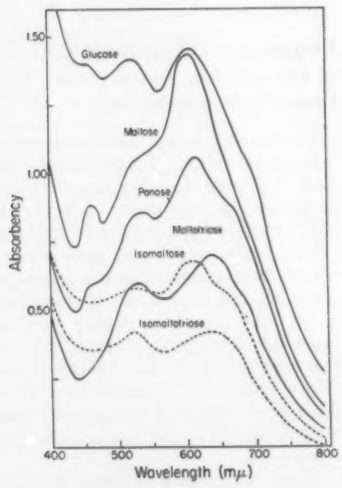


Fig. 1. Spectra (Beckmann D.U. spectrophotometer) of spots after reaction of saccharides on paper with diphenylamine-aniline-phosphoric acid reagent (*1*). Strips of paper 1 cm wide containing 150 μg of saccharide (spot 1 cm in diameter) placed in 1 cm optical cells with 0.9 cm cell spacer and held flat against optical wall of cell with proper insert. Blank cell contained paper strip cut from region adjacent to color spot. Broken lines represent isomaltose and isomaltotriose.

The presence of a minimum in the γ region (460 mμ) seemed to be characteristic of the isomaltose series, whereas only the substances containing an α, 1,4-linkage exhibited a minimum in the δ region (440 mμ). These characteristics are sharply different from those of the reaction product of diphenylamine and desoxyribose, which absorbs only at 380 mμ (*5*). Little or no differentiation in color could be obtained when the saccharides were allowed to react with the reagent in strong HCl solution. Two absorption maxima were observed, one at 510 mμ and the other at 620 mμ. Nor could large differences in color be found in the solutions obtained by extracting the spots from the paper with acetone. In the latter case, a yellow-orange residue remained on the papers from the spots of the isomaltose series, whereas no residue remained from the spots of the maltose series.

These observations suggest a competition between two reaction series, one leading to the formation of a blue product, the appearance of which does not depend on the presence of a free hydroxyl at the C-4 position of the reducing glucose, the other involving a less specific "browning" reaction that requires the presence of free C-4 hydroxyl. In this connection, Hodge has proposed that the nonenzymatic browning reaction of amines with reducing sugar goes through a dehydration reaction involving the C-4 hydroxyl (*6*).

This reagent has proved useful for distinguishing panose from isomaltose on chromatograms irrigated with the solvent mixture of Gjeisten (*7*). We have also found that the oligosaccharide spots obtained with this reagent are readily amenable to direct reflectance measurements on the developed chromatogram so that a fairly precise quantitative estimation of the oligosaccharide can be obtained. Finally, it is suggested that the spectrophotometric results and interpretations presented herein may be of value in interpreting color differences obtained with other carbohydrate series and other developing agents.

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2. We wish to thank the following individuals for generous gifts of the chromatographic standards: J. H. Pazur, maltotriose; H. M. Tsuchiya, isomaltose, isomaltotriose, and dextranase hydrolyzate of dextran [A. R. Jeanes *et al.*, *J. Am. Chem. Soc.* 75, 5911 (1953)]; R. J. Dimler, panose [M. L. Killey *et al.*, *ibid.* 77, 3315 (1955)]; and amylase hydrolyzate of amylose [R. J. Dimler *et al.*, *Cereal Chem.* 27, 488 (1950)].
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20 September 1955

## On the Rule for Leap Year

George W. Walker has suggested two changes [*Science* **123**, 25 (6 Jan. 1956)] in our present rule for leap year: first, that leap years be skipped from now until the year 2000 to bring the solstice to approximately 1 Jan.; and second, that our rule for insertion of leap year be changed. The first proposal is of academic interest only, since there is no chance of calendar reform by 1960, the first year in which he proposes that the leap year be dropped; but it is ingenious.

Walker's proposed revision of the rule for insertion of leap years is based on the assumption that the present rate of decrease in the length of the tropical year, or year of seasons, about half a second per century, will continue indefinitely. This, however, is not correct. In the course of time, the length of the year will be increasing. Astronomers working on the length of the year remind us that reasonably accurate observations are available for only about 150 years; that their work is complicated by irregularities in the length of day, some of which

are unexplained as yet; and that the error in the present Gregorian rule should amount to a day only after some 3000 years. They suggest that by that time the length of the year, and changes in it, should be known much more accurately than at present. Hence, they have recommended leaving revision of the Gregorian rule to future generations.

The Gregorian rule for leap year is "Years divisible by 4 are to be leap years unless they are also divisible by 100, in which case they are to be leap years only if divisible by 400." This rule obviously expresses the length of the year in days as

$$365 + \frac{1}{4} - 1/100 + 1/400$$

or in decimals as

$$365 + 0.25 - 0.01 + 0.0025$$

Combining, we obtain 365.2425 as the length of the Gregorian year.

The true length of the tropical year is 365.24220. Comparing with the Gregorian year, we see that the Gregorian rule is in error by 0.0003 day per year, or 3 days in 10,000 years.

Walker proposes the rule "Years divisible by 4 are to be leap years unless they are also divisible by 120, in which case they are to be common years." This expresses the length of the year in days as

$$365 + \frac{1}{4} - 1/120$$

or in decimals

$$365 + 0.25 - 0.00833 \ldots$$

Combining, we obtain 365.24166 . . . as the length by the proposed rule. Comparing this length, 365.24166 . . . , with the adopted length 365.24220, we see that it is too short by more than 5 days in 10,000 years.

Since both the Gregorian rule and the proposed rule start with "Years divisible by 4 are to be leap years . . ." one applying either rule starts with a mental division of the last two figures of the year number, to see whether it is divisible by 4. For the next step, almost any high-school student who has read the Gregorian rule recently should be able to figure mentally that the century years 1800, 1900, and 2100 are not divisible by 400 and, hence, are leap years; but 2000 is divisible by 400 and, hence, is not a leap year. The Gregorian rule can be applied mentally, but how many high-school students would be able to figure without pencil and paper which years between 1900 and 2100 are divisible by 120 and, hence, would not be leap years by the proposed rule?

There have been many proposals for correcting the Gregorian rule, but the only one usually mentioned in textbooks on astronomy was proposed several generations ago. It is that "but years divisible by 4000 shall not be leap years" be added to the Gregorian rule. This would make the length of the calendar year 365.24225 days and, on the assumption that the present figure for mean length of the year of seasons is correct, reduce the error to half a day in 10,000 years. This rule also continues the use of the division by 4, and has no effect on the present rule before the year 4000.

It has been suggested also that, if it develops that our present figure for the mean length of the year is appreciably too large, "but years divisible by 2000 shall not be leap years" be added to the Gregorian rule. This should be applied first in the year 2000; with our present marvelously accurate crystal clocks, astronomers may well know before the year 2000 whether this addition would improve the rule.

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16 January 1956

## Determination of Phosphocreatine and Other Phosphorylated Intermediates with Dowex-1 Resin

The analysis of phosphocreatine (PCr) in animal tissues has long been beset with certain difficulties. Interfering labile substances such as phosphopyruvate and triose phosphates are usually present in various amounts. In addition, the problem of isolating phosphocreatine chemically for radioactive studies is particularly acute since the laborious technique of removing orthophosphate (P) by magnesium precipitation (*1*) results in a loss of PCr and other compounds. Paper chromatography (*2*) has been used, but resolution is poor and spontaneous hydrolysis is a problem. The present report describes the use of the anion exchange resin Dowex-1 in the quantitative separation of PCr. Dowex-1 resins have been extensively applied to the analysis of nucleotides (*3, 4*), but little attention has been given PCr and other phosphorylated intermediates.

After the discovery that hydrolysis of labile phosphates occurred more readily with finer mesh resins (200 to 400 mesh), a porosity of 100 to 200 mesh Dowex-1 X8 resin was employed and the elution was performed at 0°C. The resin, which was stored in concentrated formic acid, was washed in 6 by 0.7-cm columns with 10 volumes of concentrated formic acid (plus 1*M* ammonium formate if other intermediates were to be separated) and then with distilled water until the effluent was neutral. After the neutralized extract was run through, the column was washed with 10 ml of water. Elution of the phosphorylated intermediates was begun with 0.05*N* formic acid, and the collection rate was 5 ml/10 minutes per tube, using the automatic fraction collector.

A typical separation of some intermediates is presented in Fig. 1. With the exception of hexose phosphates, most of the other substances are clearly separable. There is a tendency for most hexose phosphates as well as phosphoglyceric acid to be eluted simultaneously. At present, some success in separation has been achieved by combining silicic acid with Dowex-1. When only PCr was to be

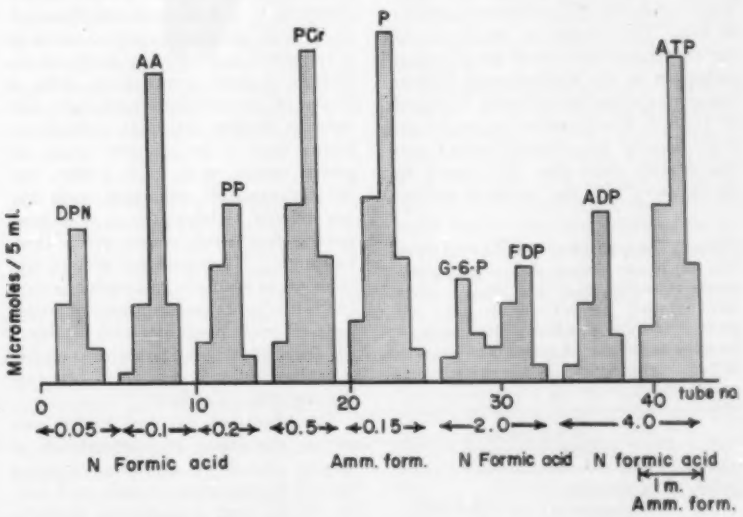


Fig. 1. Separation of some phosphorylated intermediates by ion-exchange chromatography. DPN, diphosphopyridine nucleotide; AA, adenylic acid; PP, inorganic pyrophosphate; PCr, phosphocreatine; P, orthophosphate; G-6-P, glucose-6-phosphate; FDP, fructose-1,6-phosphate; ADP, adenosinediphosphate; ATP, adenosinetriphosphate. Further details of the method are described elsewhere (*5*).

Table 1. Phosphocreatine of mouse tissues as determined by chemical and chromatographic methods. Mice were thrown into a dry ice-acetone mixture and tissues were removed in frozen state with chisel and hammer. Values are expressed in micromoles per gram of wet tissue and are an average of four determinations varying within 8 percent.

| Tissue | Method | | |
|---|---|---|---|
| | Chemical | Chromatographic | Chromatographic (unfrozen) |
| Skeletal muscle | 6.48 | 5.75 | 5.15 |
| Brain | 3.05 | 4.25 | 3.00 |
| Kidney | 3.80 | 3.67 | 3.15 |
| Liver | 2.75 | 1.96 | 2.00 |

analyzed, the column was washed with 25 ml of 0.05*N*, followed by 25 ml of 0.15*N* formic acid before elution of the PCr with 0.5*N* formic acid. Presumably no other known phosphorylated intermediates are eluted with 0.5*N* formic acid. Inorganic pyrophosphate (PP), which is usually removed with 0.15*N* formic acid, if present, could be removed by collecting an additional 10 to 20 ml with 0.15*N* acid.

A number of tissues have been analyzed for PCr by both the chemical and chromatographic technique (Table 1). In general, the agreement between both methods is good, although the values are usually higher with the latter method. Tissues removed without rapid freezing of the whole animal had somewhat lower values for PCr, with the exception of liver. The reason for preference of the chromatographic over the chemical technique in the separation of PCr in isotopic experiments is clearly indicated in Table 2. The variation in specific activity among two determinations was considerably more than 100 percent in all instances with the chemical method and less than 25 percent with the chromatographic method, with the exception of liver. Preliminary studies reveal that the phosphocreatine of liver varies considerably, depending on the nutritional state of the animal.

Table 2. Comparison of specific activity of PCr of mouse tissues determined chromatographically and chemically. Mice were injected intraperitoneally with 100 μc of $P^{32}$ (orthophosphate) and sacrificed 30 minutes later. Each value is an average of two determinations in two separate experiments.

| Tissue | Specific activity (counts/min μmole P) | |
|---|---|---|
| | Chromatographic | Chemical |
| Kidney | 9,700, 8,500 | 15,000, 6,000 |
| Brain | 705, 950 | 200, 1,500 |
| Liver | 9,650, 18,000 | 4,500, 12,000 |
| Muscle | 1,680, 2,050 | 1,500, 3,800 |

The present chromatographic method has been successfully used in the separation of PCr and other phosphorylated intermediates in phosphorylation studies with isolated frog nerve (*5*) and mouse brain *in vivo* (*6*). In addition to being quantitative, the method is rapid and simple, especially, when merely P and PCr are to be analyzed. A manifold with as many as six outlets has been successfully used to operate an equal number of columns from a common reservoir, either by hand or with an automatic fraction collector (*7*).

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7. This work was supported by the Office of Naval Research.

22 September 1955

## Biological Effect of Hydroxylysine

Although it is well established that hydroxylysine (2,6-diamino-5-hydroxyhexanoic acid) occurs regularly in collagens of terrestrial and marine animals and the gelatins derived from these, little is known of its biological significance. Despite its obvious structural similarity to lysine, there is no evidence in the reported results of *in vivo* studies that the hydroxylated compound is in any way related metabolically to this more widely distributed amino acid. Thus, Lindstedt (*1*) reported that dietary supplements of synthetic hydroxylysine were ineffective in promoting growth of lysine-deficient rats. Bergstrom and Lindstedt (*2*) found that hydroxylysine was unable to replace lysine for growth of *Leuconostoc mesenteroides* P-60.

The results of our own studies concerning the ability of hydroxylysine to support growth of the lysine-requiring bacteria *Streptococcus faecalis* (A.T.C.C. No. 9790) and *Leuconostoc mesenteroides* P-60 (A.T.C.C. No. 8042) are in general agreement with those of the afore-mentioned workers in that the addition of hydroxylysine to a lysine-free medium failed to allow growth of either of these organisms. However, while hydroxylysine was unable to support growth in the complete absence of lysine, it appeared to have considerable ability to lower the lysine requirements of these bacteria. Some typical results illustrating this effect are given here.

The composition of the lysine-free basal medium and the techniques for measurement of growth responses of the organisms to increments of lysine were the same as those described by Henderson and Snell (*3*). The L-lysine HCl and racemic hydroxylysine HCl used in this work were synthetic products (*4*). Hamilton and Anderson reported (*5*) that racemic hydroxylysine from the same source contained approximately 40 percent hydroxy-DL-lysine and 60 percent allohydroxy-DL-lysine. The results in Fig. 1 show the effects of additions of 2, 20, and 1000 μg of racemic hydroxylysine per milliliter of double-strength basal medium on the responses of *Streptococcus faecalis* to increments of lysine.

It is evident that the presence of only 2 μg of the racemic hydroxy compound (supplying only about 0.4 μg of the natural isomer) per tube gives an apparent reduction of more than 20 μg in the amount of L-lysine required for half-maximum growth of the organism. This suggests that hydroxylysine has some effect other than, or in addition to, that of serving as a nutrient that can, under conditions of suboptimal lysine supply, be converted into lysine or be exchanged for lysine in protein synthesis.

Somewhat similar effects of hydroxylysine addition to the basal medium on the apparent lysine requirement of *Leuconostoc mesenteroides* P-60 were observed, using the method of testing described in a previous paragraph. However, with this organism, the relationship between apparent lysine requirement and hydroxylysine concentration is more complex. Although small amounts of hydroxylysine allow maximum growth of the organism at reduced levels of lysine,

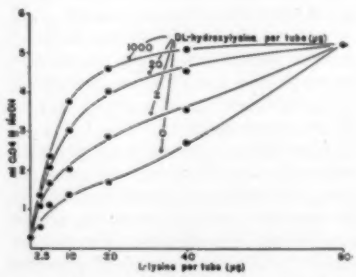


Fig. 1. Effect of addition of racemic hydroxylysine to the basal medium on the response of *Streptococcus faecalis* to increments of L-lysine.

high levels of the hydroxy compound (1 or 2 mg per tube) show a marked growth-depressing effect. This growth depression by high levels of hydroxylysine is eliminated by addition of larger amounts of L-lysine.

Both *Leuconostoc mesenteroides* P-60 and *Streptococcus faecalis* are commonly used for microbiological assay of lysine in hydrolyzates of foods and tissues and each of these organisms has been accepted, on the basis of earlier work (*6*, *7*), as having a highly specific requirement for lysine. However, in view of the results reported here, it seems likely that the presence of hydroxylysine in sample hydrolyzates could interfere with the quantitave microbiological determination of lysine when these organisms are used with basal media that contain no hydroxylysine.

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2. S. Bergstrom and S. Lindstedt, *Acta Chem. Scand.* **5**, 157 (1951).
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13 September 1955

## What Are Variables and Constants?

The notion *variable* has not in the literature attained the degree of clarity that would justify the almost universal use of that term without explanations. Recent investigations (*1*) have resolved it into an extensive spectrum of meanings, some pertaining to reality as investigated in science, others belonging to the realm of symbols studied in logic—two altogether different worlds. As a corollary, these distinctions yield a clarification of the notion *constant*.

*Science and applied mathematics.* By *quantity* we mean a pair of which the second member (or *value*) is a number while the first member (or *object*) may be anything. We call a class of quantities *consistent* if it does not contain two quantities with equal objects and unequal values. If $p(\gamma)$ denotes the pressure (in a chosen unit) of a gas sample $\gamma$ (*2*), then the pair $[\gamma, p(\gamma)]$ is a quantity, and the class of all such pairs for any $\gamma$ is consistent. This class reflects the physicist's idea of gas pressure, $p$. Gas volume, $v$, and temperature, $t$, can be defined similarly. Consistent classes of quantities, such as $p$, $v$, and $t$, are what scientists and mathematicians in applied fields mean by *variable quantities* and what Newton called *fluents*. The class of all gas samples will be referred to as the *domain* of $p$; the class of all numbers $p(\gamma)$ as the range of $p$.

A variable quantity whose range consists of a single number is said to be *constant*. An example is the gravitational acceleration $g$ at a definite point on the earth, defined as the class of all pairs $[\alpha, g(\alpha)]$ for any object $\alpha$ falling in a vacuum, where $g(\alpha)$ denotes the acceleration of $\alpha$. For any $\alpha$, this value of $g$ is found to be equal to one and the same number, g. (Throughout this paper, symbols for fluents are italicized and symbols for numbers are printed in roman type.) A less important, because less comprehensive, example is the distance traveled by a specific car C while C is parked. (The distance traveled by C is the class of all pairs $[\mu, m(\mu)]$ for any act $\mu$ of reading the mileage gage in C, where $m(\mu)$ is the number read as the result of $\mu$.

In a plane, the coordinates relative to a chosen Cartesian frame are variable quantities whose domain is the class of all points (*3*). The abscissa $x$ is the class of all pairs $[\pi, x(\pi)]$ for any point $\pi$. In the equation of the straight line $x - y = 3$ the *3* denotes the constant fluent consisting of the quantities $(\pi, 3)$ of value 3 for each point $\pi$.

Of paramount importance are the consistent classes of quantities whose domains consist of numbers. An example is the class of all pairs $[x, \log x]$ for any number $x > 0$, called the logarithmic function or the function *log*. It is capable of connecting consistent classes of quantities—for example, $y = \log x$ along a logarithmic curve, and $w = \log v$ for an isothermic expansion of an ideal gas, if $w$ denotes the work in a proper unit. That is to say, $y(\pi) = \log x(\pi)$ and $w(\gamma) = \log v(\gamma)$ for any point $\pi$ on the curve and any gas sample $\gamma$ pertaining to the process. Moreover, *log* connects functions—for example, the exponential with the identity function, and *cos* with *log cos*. Because of their connective power, functions are omnipresent in science as well as in mathematics (*4*). Variable quantities such as $p$ and $v$ (whose domains do not contain numbers or systems of numbers) lack this power and therefore are confined to special branches of science such as gas theory. Denying the significance of this difference would be denying the role of mathematics as a universal tool in quantitative science.

*Logic and pure mathematics.* The formula

$$3^3 - 1 = (3 + 1) \cdot (3 - 1)$$

is a statement about specific numbers designated by 3 and 1. In the more general statement

$$x^3 - 1 = (x + 1) \cdot (x - 1) \text{ for any number } x,$$

the remark "for any number x" stipulates that, in the formula, x may be replaced by the designation of any number, for example, by 3 or $\sqrt{5}$, each replacement yielding a valid statement about specific numbers. A symbol that, in a certain context and according to a definite stipulation, may be replaced by the designation of any element of a certain class is what, following Weierstrass, logicians and pure mathematicians call a *variable*. The said class is called the *scope* of the variable. The scope of x in the formula $\log x^3 = 2 \log x$ for any $x > 0$ is the class of all positive numbers. In $(\pm\sqrt{3})^4 = 9$, the symbol $\pm\sqrt{3}$ is a variable whose scope consists of the two numbers $\sqrt{3}$ and $-\sqrt{3}$.

A variable whose scope consists of a single number designates that number and, in pure mathematics, is referred to as *a constant*. Examples include numerals (1, 3, . . .); e, designating the base of natural logarithms; and brief designations of numbers with unwieldy symbols, such as $2^{\sqrt{2}} + e^{e^2}$—abbreviations introduced for the purpose of just one discussion involving repeated references to that number. As such *ad hoc* constants, one customarily uses the letters a, b, c, . . . , which, just as x and y, serve as variables in other contexts, for example, in the statement involving two variables

$$x^2 - a^2 = (x + a) \cdot (x - a) \quad \text{for any x and any a.}$$

Because of its vicarious character, a variable may always be replaced, without any change of the meaning, by any otherwise unused letter, for instance, a by y or x by b.

Variables whose scopes are classes of numbers are called *numerical variables*. The definitions of $p$ and $g$ make use of variables $\gamma$ and $\alpha$ whose scopes consist of gas samples and falling objects, respectively. Statements that are valid for many fluents are conveniently expressed in terms of *fluent variables*; for example,

$$\text{If } z = \log u, \text{ then } dz/du = 1/u \quad \text{for any two fluents } u \text{ and } z \qquad (1)$$

In Eq. 1, $u$ and $z$ may be replaced by $x$ and $y$: if $y = \log x$ (which holds along the logarithmic curve), then $dy/dx = 1/x$; or by $v$ and $w$: if $w = \log v$ (which holds for an isothermic expansion), then $dw/dv = 1/v$. But $u$ and $z$ in Eq. 1 must not be replaced by numbers such as e and 1: although $1 = \log e$ is valid, $d1/de = 1/e$ is nonsensical.

*Confusion in the literature.* No clear distinction has heretofore been made between numerical and fluent variables. Moreover, in the literature, numerical variables and variable quantities, not-

withstanding the profound differences between them, are indiscriminately referred to as "variables"; and the two concepts have actually been confused. For instance, numerous attempts (*5*) have been made to define gas pressure as a symbol that may be replaced by any value of pressure, thus as a numerical variable, p, whose scope is the range of what herein has been called the fluent $\dot{p}$. But a fluent is not determined by its range. Could Boyle have connected pressure and volume on the basis of mere information about the ranges of $\dot{p}$ and $\dot{v}$? It was by transcending these ranges and referring to the domains, namely, by comparing $v(\gamma)$ and $p(\gamma)$ for the same sample $\gamma$, that he discovered $v(\gamma) = 1/p(\gamma)$ (in proper units) for any $\gamma$ of a certain temperature or, without reference to a sample variable, $v = 1/p$. Neither formulation involves numerical variables. Boyle's Law connects specific fluents.

Analogously, constant fluents have been identified with their numerical values even though what primarily interests the physicist in gravitational acceleration clearly is the fact that g is its value for any $\alpha$ rather than the number g as such.

Numerical variables and variable quantities belong to worlds that are not only different but nonisomorphic. The former are interchangeable, the latter are not:

$$x^2 - 4y^2 = (x + 2y) \cdot (x - 2y) \text{ and}$$
$$y^2 - 4x^2 = (y + 2x) \cdot (y - 2x)$$

for any x and y are tantamount. But $x - y = 3$ and $y - x = 3$ are different straight lines and $w = log\ v$ is incompatible with, and not tantamount to, $v = log\ w$.

Only the consistent maintenance of all these distinctions makes it possible to formulate mathematical analysis as well as its applications to science as a system of procedures following articulate rules (*6*).

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1. Compare K. Menger, "The ideas of variable and function," *Proc. Natl. Acad. Sci. U.S.* 39, 956 (1953) and "On variables in mathematics and in natural science," *Brit. J. Phil. Sci.* 5, 134 (1954). A paper "Random variables and the general theory of variables" is in print *Proc. 3rd Berkeley Symposium Math. Statistics* (1955). A systematic exposition of the new theory of variables is contained in K. Menger, *Calculus. A Modern Approach* (Ginn, Boston, 1955).
2. The term *gas sample* means gas in a specific container at a definite instant.
3. Depending on whether a physical, a postulational, or a pure plane is under consideration, a "point" is a physical object (for example, an ink dot in a paper plane), or an undefined object satisfying certain assumptions, or an ordered pair of numbers.
4. Even if, following the suggestion of some mathematicians, one called all consistent classes of quantities "functions," one obviously would need a special term for "functionally connecting functions" such as *log*.
5. Compare, for example, R. Courant, *Differential and Integral Calculus* (Interscience, New York, 1954), vol. 1, p. 14.
6. Compare K. Menger, *Calculus. A Modern Approach* (Ginn, Boston, 1955).

9 September 1955

## Prenatal Diagnosis of Sex Using Cells from the Amniotic Fluid

In most mammals, including human beings, males normally have the sex chromosome constitution XY, and females the sex chromosome constitution XX (*1*). It has been shown in a variety of tissues in human beings and some other species (*2*) that there is a sex difference in the percentage of cells with chromocenters, especially those at the nuclear membrane; this presumably is due to this difference in sex chromosome constitution in males and females. A determination of the percentage of cells with chromocenters can therefore give, in sexually normal individuals, a diagnosis of sex.

The present study was undertaken in order to show whether, in human beings, such a diagnosis can be made before birth, not only for aborted fetuses from which pieces of tissue can be removed for examination, but also for viable fetuses by an examination of cells from the amniotic fluid. In order to establish whether amniotic fluid contains cells suitable for diagnosis, fluid was taken before delivery by puncture of the membranes from women in the ninth month of pregnancy. The fluid was centrifuged, and the cells were smeared on slides, fixed in alcohol-ether, and stained with Feulgen and fast green (Fig. 1).

Our analysis has shown that cells suitable for the diagnosis are present, and an examination of 35 cases in the ninth month, which include those reported previously (*3*), has given 35 correct diagnoses of the sex of the fetus.

It therefore seems that this method is particularly reliable, especially since there appears to be no theoretical objection to it. The only apparent exception that occurs to us at present is the rare case of an intersex in which the sexual phenotype does not correspond to the sex chromosome constitution. When one is collecting the amniotic fluid it is, of course, essential to avoid contamination with cells from the mother.

Amniotic fluid can be obtained from viable human fetuses from 12 weeks to term (*4*). We have found, from an examination of the fluid obtained from

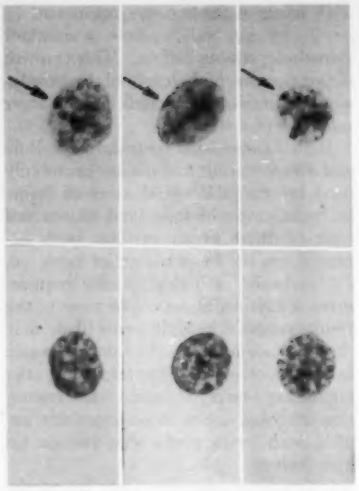

Fig. 1. Photomicrographs of cells from the amniotic fluid (×1500). (Top row) Nuclei with a chromocenter at the nuclear membrane; from female human fetuses in the ninth month. (Bottom row) Nuclei without a chromocenter; from male human fetuses in the ninth month.

viable human fetuses in the sixth and seventh months, that a prenatal diagnosis of sex can be made at these stages. We have also found suitable cells in the fluid of an aborted 8-week-old human embryo.

It may be possible to apply this method for the prenatal diagnosis of sex to domestic animals.

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30 December 1955

# Book Reviews

**Research Films in Biology, Anthropology, Psychology, and Medicine.** Anthony R. R. Michaelis. Academic Press, New York, 1955. xvi + 490 pp. Illus. $10.

In the publication of this book, investigators as well as teachers in the biological sciences (including anthropology, psychology, and medicine) have a source of detailed, technical information that should enable beginners to begin to use and advanced workers more effectively to use cinematography. The book does not deal too exclusively with specific apparatus and, for this reason, it is not "dated." Rather, it is written to inform the reader in the general principles of the theory and art of cinematography. It is not a catalog of apparatus, yet it is a source of information about what general types of apparatus have been put together by scientists for the solution of their special problems and so may furnish suggestions for other installations.

The book is divided into three parts: 114 pages on the biological sciences (including such problems as bacterial growth and reproduction, tissue culture, embryology, locomotion, feeding mechanisms, circulation, nerves and sense organs, plant growth, tropisms, plant physiology, mycology, animal behavior); 91 pages on the "human sciences" (largely anthropology, psychology, and psychiatry); and 99 pages on the "medical sciences."

In each part Michaelis goes over the use of cinematography, reviewing some films already made. He discusses various special considerations in the area (for example, in animal behavior, the need for working in infrared for certain purposes). He then gives a comprehensive account of the application of cinematography in the main fields of research. For example, in the "medical sciences," applications of cinematography described are to external conditions, surgery, cavity exploration, x-ray analysis, locomotion, digestion, respiration, genitourinary system, circulation, sense organs, nervous system, pathology, and aviation medicine. In each case the scientific result revealed or elucidated by the use of cinematography is emphasized. There are thoroughly adequate and ample specific references throughout the text to a bibliography of 1490 titles.

I have had many years of experience with many kinds of cinematographic problems in biology, and I can say with full assurance that this book is the best in its field. Moreover, it should be a model for writers of "how-to" books—there is a fine balance between the treatment of the problem to be solved and the method of solving it. Unlike so many books on photography, the author of *Research Films* has a good grasp of, and a feeling for the biologist's point of view and language. The illustrations are excellent; the index is adequate.

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**Principles and Applications of Physics.** Otto Blüh and Joseph D. Elder. Interscience, New York, 1955. xiv + 866 pp. Illus. $7.

The turnover of physics textbooks in most western European countries has been much smaller than in the United States with its larger population of college-attending youth. Perhaps this is one reason why many textbooks of European origin are too encyclopedic to gain ready acceptance as required books in American universities. The book under review is based in part on Otto Blüh's earlier writing in Europe; it is considerably larger than most American textbooks. It is a mine of information addressed to the intelligent student who is expected already to have mastered some elementary physics. Without such a background, the pace at which the book proceeds would discourage the average student.

In the preface the authors express the hope that their book will have almost universal utility. "The text is adaptable to a one-year lecture course, when a selection of material according to the special requirements of the class will be necessary, but it contains ample material for a two-year course of which approximately one year would be devoted to classical, the other to modern physics. . . . Applications of physics have been adequately discussed as illustrations of the basic principles involved." In writing this book the authors "have attempted to fill the gap between elementary and advanced specialized textbooks." Following one of the senior author's special interests "consideration has been given . . . to the biologic, medical and radiological applications of physics . . . at the same time the text should provide for students of applied science and engineering a wider understanding of physics in conformity with the demands for the replacement of technical physics by basic . . . physics . . . . The integrating features of the book may perhaps also claim the interest of the graduate physics student, of the physics teacher . . . and of the scientists-at-large."

At a time when the proper teaching of physics is undergoing keen scrutiny, both by people within and without the physics profession, the authors have courageously written a book in which the traditional order and emphasis are not followed. Altogether it consists of 10 parts of somewhat unequal lengths dealing with the following: I, "Methods of physics, mathematics"; II–VI, "Basic concepts, mechanics, energy, fields, oscillations, thermodynamics"; VII - IX, "Corpuscles, atomic and nuclear physics"; X, "Scope and importance of the physical sciences."

In places the treatment is somewhat too condensed to be easily followed by a student who meets a topic for the first time. Teachers will certainly enjoy the volume, particularly part X. A junior or senior undergraduate major in physics might well put Blüh and Elder's volume on his list of Christmas or birthday wants and read it during his summer vacation.

The type face is large and clear; a few of the halftones (except for 10 or 12 plates) leave something to be desired; and the black cover is unattractive. But the book is an extremely good value at the price.

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**Chemistry of the Soil.** Firman E. Bear, Ed. Reinhold, New York, 1955. x + 373 pp. Illus. $8.75.

This monograph brings together a great part of the factual material needed for an understanding of the chemical nature of soils. Ten well-chosen areas (chapters) make it possible to present the significant facts of soil chemistry without serious overlapping. The authors of the chapters are well known through their contributions to the subject.

Soil development, by Barshad, deals with the methodology for interpreting soil-profile development in terms of the effect of developmental factors on parent material. Chemical composition, by Lawton, covers the gross elemental composition of primary minerals and soils.

Soil colloids are described by Toth through their schematic crystal structures and ion-exchange properties. But the exchange phenomena itself is rather thoroughly and competently explored in a separate chapter, by Wiklander, dealing with ion-exchange formulas, the Donnan equilibrium, membrane potentials, amphoteric reactions, and ion-exchange reactions between solids.

The chapter on soil organic matter, by Fraser, discusses plant constituents and their decomposition products. Kardos discusses soil fixation of plant nutrients and the chemical reactions involved that have special implications in soil fertility. Oxidation-reduction processes with respect to soil development and fertility are discussed by Merkle, while Thorne and Seatz cover the chemistry of acid, alkaline, alkali, and saline soils.

The world distribution of trace elements and their behavior in soils are described by Mitchell. The relationship of soil chemistry to plant nutrition, by Mehlich and Drake, forms the concluding chapter. It deals with ion adsorption by plant roots and nutrient availability as affected by soil reactions. An appendix, by Prince, on routine soil analysis is included.

Editor Bear and the authors are to be congratulated on this valuable contribution to the field of soil chemistry. Each chapter is well written and adequately documented. It is a book every worker in soil chemistry and soil fertility should possess, and it would make an excellent text or reference book for an advanced course in the principles of soil chemistry.

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**Flora of Winnebago County, Illinois.** Egbert W. Fell. Nature Conservancy, Washington, D.C., 1955. 207 pp. Cloth, $3.50; paper, $2.75.

Those concerned with the flora, vegetation, or ecology of the Middle West will be interested in this new book on one of the counties on the prairie border in northern Illinois. This book is the result of many years of careful study of the natural history of the northern part of Illinois; the author went there in 1921 to live.

The introduction is a description of the region, its geography, geology, climate, vegetation, and the range of habitats, with statistics on the geographic relationships of the components of the flora. The main part of the book is an annotated catalog of the vascular plants, with information on the local occurrence of each and interesting notes that particularly concern the plants in this county. Accompanying this are 33 pages of line drawings by the author, illustrating many of the more interesting species. A folded map in the back clarifies the local geography of the county, and a smaller map shows the areal relationships of original prairie and woodland and present-day wooded land.

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**Physics and Microphysics.** Louis de Broglie. Translated by Martin Davidson. With a foreword by A. Einstein. Pantheon, New York, 1955. 286 pp. $4.50.

This book is a collection of lectures and essays, for the most part, written, I would estimate, more than a decade ago. They suffer from the usual diseases of such a collection of much repetition and overlap. Many of the comments on the most recent scientific developments are seriously out of date, in spite of valiant efforts by the translator in the form of notes.

The book is divided into three parts. In the first, entitled, "Science," the author describes recent developments in science with special emphasis on wave mechanics, nuclear physics, and relativity. A historical approach is employed. These chapters are very lucidly written and can be understood by the nonspecialist, although they contain very little that is new for a competent physicist. The second section is entitled "Scientific philosophy." Here there is much emphasis on the comparison of space and time in classical and quantum physics and the relationship of this question to the wave-particle dualism.

One does not always agree with de Broglie, but his ideas are very interesting and thought-provoking. The road to a great discovery is not an easy one, but, as de Broglie points out in an essay on personal memories of the beginning of wave mechanics, a discovery such as the one he made presents many problems of understanding before it can become completely useful. He discusses the blind alleys he followed in an essay of great interest to me and, I am sure, to other physicists as well as to students of the history of science.

Another chapter in this section that is most ably presented is entitled, "The grandeur and moral value of science." On the other hand, the chapter on the relationship of modern science and the philosophy of Bergson was rather disappointing, probably because only a summary of the chapter is presented and is therefore much too sketchy to be satisfying. There are, however, many other hints throughout the book on the parallels between Bergson's philosophy and modern physics, which I hope de Broglie will someday discuss more extensively in a separate volume.

The third section is entitled "History of the sciences" and contains essays on the future of physics, the relationship of pure and applied science, a sketch on the history of the radio, and finally some remarks on nuclear energy, which, when one remembers that they were written before the explosion of the first atomic bomb, are remarkably prescient.

The book will prove to be of interest to the nonphysicist, who will find not only the philosophy of modern physics very clearly discussed but also such very important matters as the relationship between science and the scientist, between science and applied science, and between science and society illuminated by cogent and stimulating concepts.

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**Ordovician Cephalopod Fauna of Baffin Island.** Memoir 62. A. K. Miller, Walter Youngquist, and Charles Collinson. Geological Society of America, New York, 1954. vii + 234 pp. Illus. + plates.

The publication of this volume in the memoir series of the Geological Society of America is very timely, in addition to being intrinsically valuable, because of current special activity of the Geological Survey of Canada in exploration of the arctic region, including Baffinland. Several field parties working in Baffinland in the summer of 1955 have added materially to knowledge of areal geology and structure; a preliminary report on this work is now in preparation.

The study by Miller and coauthors is concerned primarily with the characters exhibited by 23 genera of nautiloid cephalopods obtained from a single locality (Silliman's Fossil Mount) near the southeastern extremity of Baffinland. Brief descriptions and excellent illustrations of various brachiopods, corals, and the widely distributed spongelike fossils (*Receptaculites*) are given also, and the volume contains a report on 23 species (four new genera and subgenera) of trilobites (by H. B. Whittington) as well

as short sections on graptolites (by C. E. Decker and fossils in Paleozoic rocks near the main fossil locality (by Y. O. Fortier).

Main interest attaches to the age of the fossil-bearing formations and content of the faunal assemblage. Based on occurrence together of some supposed Late Ordovician (Richmond) species with forms that elsewhere predominantly occur in Middle Ordovician (Trenton) strata, the cephalopod assemblage is interpreted to signify an early part of Late Ordovician times. Other fossils, especially the trilobites, point less ambiguously to Trentonian age.

New paleontological information obtained from the northern margin of the North American continent is not only furnishing basis for accurate interpretation of the geologic history of this region but may contribute importantly to understanding paleontological features of formations in the interior of the continent.

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**Basic Mathematics for Science and Engineering.** Paul G. Andres, Hugh J. Miser, and Haim Reingold. Wiley, New Work; Chapman & Hall, London, 1955. vii + 846 pp. Illus. $6.75. (A revision of *Basic Mathematics for Engineers,* 1944.)

This textbook is proposed for a unified freshman year of mathematics work to include algebra, trigonometry, and analytic geometry. It is an adequate basis for the study of the calculus and is directed, as its title states, to students in science and engineering. This is a revision of an earlier volume by the same authors. Considerable space (about 100 of the 800 pages) is given to prerequisite high-school mathematics so that students may have ready access thereto. This review material is unusually well treated with emphasis on radicals and exponents, fractions, and solution of equations. There is an abundance of word problems, many of an unusual form; and manipulation of many formulas with other variables besides $x$ and $y$ is carefully included.

The usual material in college algebra, trigonometry, and analytic geometry is adequately covered. The authors are to be congratulated on a careful analysis of important material and on the omission of certain topics that still appear in many textbooks *only* because of tradition. For example, the solution of certain oblique triangles by the law of tangents or half-angle formulas is replaced by the use of the laws of sines and cosines—a commendable feature in this day of electric desk calculators. Reference is frequently made to applications in science and engineering with the primary purposes of stimulation in study and of bridging the gap between mathematics and its utilization. As a second example of these authors' analysis, the solution of simultaneous linear equations is treated by the Doolittle method; hence, in the study of determinants, the students should realize that they are concerned beyond the mere solution of three or four equations in as many variables. The theory of determinants, so requisite to matrix theory and to computer theory, is covered only for second- and third-order determinants but more competently than is usual; evidently the belief of the authors is that students can learn the theory for the general order more thoroughly and easily in a later course.

I would have preferred more emphasis in analytic geometry on the locus derivation and, consequently, on fewer boldface formulas (which really do not need to be memorized). The treatment of solid analytics is too brief (31 pages in all), and cylindrical and spherical coordinates are omitted.

The slide rule is treated in the first chapter; far fewer problems than usual follow in the text with trick numbers of solutions. This is both commendable and desirable, for the psychological attitude of expecting simple answers is an inevitable but unfortunate consequence of study with many textbooks.

This textbook, then, is of some significance in the current trend of experimentation that is so important if mathematics instruction is to be progressive and not static. I wish that some other way could be found to cope with the inadequate preparation of the entering student than to make the requisite material available for reference in a college-level textbook; certainly improvements in education in the high school must occur if college instruction is to yield more and better trained students in science and engineering.

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## Books Reviewed in The Scientific Monthly, April

*Plant Taxonomy,* E. L. Core (Prentice-Hall). Reviewed by L. Constance.

*Quantitative Analysis,* A. F. Daggett and W. B. Meldrum (Heath). Reviewed by A. D. Bliss.

*Advanced Calculus,* A. E. Taylor (Ginn). Reviewed by A. W. Hobbs.

*The Botany of Cook's Voyages and Its Unexpected Significance in Relation to Anthropology, Biogeography and History,* E. D. Merrill, vol. 14, No. 5/6 (Chronica Botanica; Stechert-Hafner). Reviewed by J. M. Fogg, Jr.

*Die Binnengewässer in Natur und Kultur.* A. Thienemann (Springer). Reviewed by A. D. Hasler.

*Rome beyond the Imperial Frontiers,* M. Wheeler (Philosophical Library). Reviewed by M. H. Adams.

*Fact, Fiction, and Forecast,* N. Goodman (Harvard Univ. Press). Reviewed by R. J. Seeger.

*Contributions to Plant Anatomy,* Irving W. Bailey (Chronica Botanica; Stechert-Hafner). Reviewed by J. Philpott.

*Introduction to Social Welfare,* W. A. Friedlander (Prentice-Hall). Reviewed by W. W. Boehm.

*The Unified System Concept of Nature,* S. T. Bornemisza (Vantage). Reviewed by G. Hardin.

*Sir Joseph Banks, the Autocrat of the Philosophers, 1744–1820,* H. C. Cameron (Batchworth). Reviewed by J. Ewan.

*The Luminescence of Biological Systems,* F. H. Johnson, Ed. (AAAS). Reviewed by C. E. ZoBell.

## Miscellaneous Publications

*(Inquiries concerning these publications should be addressed, not to* Science, *but to the publisher or agency sponsoring the publication.)*

*Informe de la Tercera Conferencia sobre los Problemas de Nutrición en la América Latina.* Held at Caracas, Venezuela, 19–28 October 1953. Publicaciones Científicas No. 12. Oficina Sanitaria Panamericana, Washington 6, 1954. 54 pp.

*The Sergestidae of the Great Barrier Reef Expedition.* Great Barrier Reef Expedition 1928–29, Scientific Reports, vol. VI, No. 5. Isabella Gordon. 11 pp. 5s.

*The Otiorrhynchine Curculionidae of the Tribe Celeuthetini (Col.).* Guy A. K. Marshall. 134 pp. 35s. British Museum (Natural History), London, 1956.

*Learning about Tests.* Junior Life Adjustment Booklet. Joseph C. Heston. Science Research Associates, Chicago 10, 1955. 40 pp. $0.50.

*The Report of the Principal to the Trustees and Ten-Year Reports of the Department Chairmen.* vol. 52, No. 1, of *Phillips Exeter Bulletin.* Phillips Exeter Academy, Exeter, N.H., 1955, 61 pp.

*Handbook of Toxicology.* vol. I. WADC Tech. Rept. 55–16. William S. Spector, Ed. Wright Air Development Center, Wright-Patterson Air Force Base, Ohio, 1955. 408 pp.

*Lung Function in Coalworkers' Pneumoconiosis.* Medical Research Council Rept. Ser. No. 290. J. C. Gilson and P. Hugh-Jones. Her Majesty's Stationery Office, London, 1955. 266 pp. $3.78.

*Cytotaxonomic Studies in Allium.* I, *The Allium canadense Alliance.* Research Studies of the State College of Washington, Monographic Suppl. No. 1. Marion Ownbey and Hannah C. Aase. State College of Washington, Pullman, 1955. 106 pp. $2.

# Scientific Meetings

## Calorimetry

More than 100 scientists from government, academic, and industrial laboratories in the United States and Canada participated in the tenth annual Calorimetry Conference held at the University of Minnesota, Minneapolis, 16–17 Sept. 1955. The program, arranged by Edgar F. Westrum, Jr. (University of Michigan) under the chairmanship of Warren DeSorbo (General Electric Research Laboratory), featured individual reports and general discussions or recent results and new techniques of precision calorimetry.

After a brief welcoming address by L. H. Reyerson of the University of Minnesota, the second Hugh M. Huffman Memorial lecture was delivered by F. G. Brickwedde (National Bureau of Standards). His timely subject, "Thermometry in relation to calorimetry," explained the correction of precise calorimetric data to the thermodynamic scale, the reliability and accuracy of temperature scales currently employed, and the recommendations of the 1955 Paris International Conference on Low Temperature Physics regarding the adoption of temperature scales for the liquid helium region. J. R. Clement and J. K. Logan (Naval Research Laboratory) reported an empirical helium vapor pressure equation valid to within ±0.002°K below the critical point.

A major emphasis of the conference concerned the heat capacity of anisotropic crystalline materials. DeSorbo summarized research progress on the measurement of the heat capacity of four specimens of synthetic and natural graphite with crystallite sizes ranging from about 100 to more than 900 angstrom units. The thermal properties of these samples revealed a definite crystallite size effect. The theoretical analysis of the lattice vibration specific heat of graphite was furthered by J. A. Krumhansl (National Carbon Research Laboratories), both with reference to the DeSorbo data and the more general problem of the normal modes. A reexamination and critical review of the vibrational spectrum and thermal properties of lamellar crystals, by Gordon F. Newell (Brown University), was followed by a round-table discussion of these topics.

Progress in the measurement of the specific heat of isotropic crystalline substances in the range of 3° to 20°K was related by W. T. Berg and J. A. Morrison (National Research Council, Ottawa). The development of a technique for studying heat capacities of small metal samples over the range 4°–12°K has been developed by Logan and Clement and applied to the study of thermal and electric anomalies in magnesium metal. D. L. Martin (National Research Council, Ottawa) reported on the determination of the heat capacities of the alkali metals (Na, K, Rb, Cs) by a continuous heating process from 20° to 310°K. Heat capacities of magnesium diboride and magnesium tetraboride from 18° to 300°K and the temperature dependence of the thermal and thermodynamic properties of these substances were reported by Robinson Swift and David White (Syracuse University). Examination of the heat capacity from 15° to 315°K and heats of fusion of the optically active alpha and beta pinene system, by H. A. McGee, Jr., and W. T. Ziegler (Georgia Institute of Technology), leads to the conclusion that the equimolar *d,l*-alpha-pinene mixture probably forms a racemic compound rather than a simple eutectic mixture.

Values of the heats of formation for some synthetic silicates of lithium, sodium, and potassium and for the minerals albite, anorthite, orthoclase, and the intervening feldspars, as well as for nepheline, leucite, synthetic diopsite and wollastonite, mineral jadeite, analcite, and a synthetic gallium anorthite ($GaAlCaSi_2O_8$) were determined by heats of solution in a calorimeter employing a 20-percent aqueous hydrofluoric acid solution operated at 74.7°C by F. C. Kracek, G. Burley, and R. J. Gordon (Geophysical Laboratory). Heats of solution and dilution have been determined for the system sodium dodecyl sulfate-water at 25°C by adiabatic calorimetry by E. D. Goddard and G. C. Benson (National Research Council, Ottawa).

Three contributions to the technique of adiabatic calorimetric measurement of thermal properties were described by University of Pittsburgh scientists. An automatic shield control device employing a series of galvanometer-photomultiplier arrangements to amplify the signals from the differential thermocouples between the calorimeter and shield and, thereby, to control the power input to the shield has been designed and constructed by M. G. Zabetakis and R. S. Craig. It completely replaces the usual manual shield control during low-temperature adiabatic calorimetric measurements. W. V. Johnston, W. E. Wallace, and Craig described modification of a conventional Brickwedde-type adiabatic calorimeter to permit its operation over the range 25° to 300°C with a precision of ±0.2 percent.

Data on the alloys $Mg_3Cd$ and $MgCd_3$ were presented with particular attention to the thermal behavior near order-disorder points. By comparison, the inadequacies of calorimeters that employ continuous heating in studying such phenomena were revealed. M. H. Aven and Craig also described a 4° to 15°K adiabatic calorimeter that employs a constant-volume gas thermometer as the working thermometer. A precision somewhat better than 1 percent was achieved in measurements on titanium and titanium hydride.

A primarily adiabatic calorimeter that may be operated isothermally was designed and constructed by E. E. Stansbury, D. L. McElroy, and G. E. Elder (University of Tennessee) for the study of stored energy in coldworked metals and alloys and other similar thermal phenomena to temperatures of 1000°C. Examples of its application to the study of the transformation in electrolytic iron, to the Curie phenomenon in nickel, and to the heat capacity of antimony-copper alloy revealed a precision of about 0.5 percent to 700°C in the measurement of heat capacity. A liquid-tin heat-of-solution calorimeter for the determination of the heats of formation of alloys constructed by Raymond L. Orr (University of California) was described. Excellent agreement between values for the heats of solution of gold and silver in liquid tin and of the heat of formation of silver-cadmium alloys in this instrument and recently reported literature values has been obtained.

A quick and simple method of correcting heat-capacity data for curvature was mentioned by Craig (University of Pittsburgh) and a treatment of calorimetric-purity data in the presence of solid-solution formation was presented by S. V. R. Mastrangelo, and R. W. Dornte (Allied Chemical and Dye Corporation).

DeSorbo, Brickwedde, and D. R. Stull reviewed progress on the temperature-scale resolution adopted by the conference in September 1954, and a new committee was selected to present the need for further investigation of these matters.

After a report by J. W. Stout on the resolution regarding the publication of thermodynamic data, the conference voted to amend the resolution to include

$(H° - H_0°)/T$ as an alternative to $(H° - H_0°)$ values in tabular summaries of thermodynamic functions and to urge utilization of the internationally adopted ice-point value of 273.15°K.

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## Southwestern and Rocky Mountain Division

The New Mexico College of Agriculture and Mechanic Arts will be host to the Southwestern and Rocky Mountain Division of the AAAS for the third time on 29 Apr.–3 May. The college is located on the eastern mesa-lands of the Rio Grande Valley in the south-central part of New Mexico. The campus is 3 miles southeast of Las Cruces and 40 miles north of El Paso, Tex., near U.S. Highway 80.

As the site of the New Mexico Agricultural Experiment Station, the Las Cruces State College community has long been one in which a high degree of interest and participation in scientific research exists. The station lies in the heart of the fertile Mesilla Valley, which is irrigated from the Caballo and Elephant Butte Dams.

Since World War II interest in science has been accelerated and augmented by the establishment and growth of a Physical Sciences Laboratory, in which more than 100 scientists and technicians engaged in basic and applied research are employed. Further impetus derives from the nearby Army Ordnance Department's White Sands Proving Grounds, since a majority of the scientific personnel, both civilian and military, of this base make their home in Las Cruces.

Edward F. Castetter (University of New Mexico) will give his retiring presidential address on Monday evening, following the annual dinner, on the subject "The vegetation of New Mexico."

The annual Powell lecture, dedicated to the memory of the noted explorer of the Grand Canyon of the Colorado River, will be given on 1 May by Seth B. Nicholson (Mount Wilson Observatory) on the timely subject "The sunspot cycle."

In view of the ever-mounting interest in our future supply of scientific workers and science teachers, a half-day panel discussion on "Education of scientists" is planned for 2 May, under the chairmanship of Anton Berkman (Texas Western College). Another half-day session will be devoted to a review of the accomplishments of the International Arid Lands Meetings held last May in Albuquerque and Socorro, N.M. Panel leaders will be Peter Duisberg, chairman of the Arid Lands Committee, and Frank E. E. Germann, secretary of the South-

Gamma emitting samples inserted into a scintillation well counter are counted by Radiation Analyzer and standard scaler. Adjustable "window" of Analyzer is set to count only pulses that fall within a pre-selected portion of the energy spectrum, thus virtually eliminating "background".

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western and Rocky Mountain Division. There will also be an open meeting of the American Rocket Society, at which a scientist of international repute will speak.

Tentative plans call for a morning session on 3 May featuring geologic and biological discussions at the White Sands National Monument, with a barbecue-type luncheon at the picnic area, followed by a tour of some of the areas of scientific interest at the Holloman Air Force (Guided Missiles) Base. Regular sessions for presentation of papers during the early days of the meeting will be grouped in the categories of botanical, zoological, social, and physical sciences.

## Meeting Notes

■ The sixth annual Rochester conference on High-Energy Nuclear Physics at the University of Rochester, 3–7 Apr., will feature major addresses by U.S. Senator Clinton P. Anderson of New Mexico, chairman of the Joint Congressional Committee on Atomic Energy, and Robert Oppenheimer, director of the Institute for Advanced Study, Princeton, N.J.

More than 150 of the world's leading physicists from the principal research laboratories of this country and from about 16 foreign nations have been invited to attend the conference. It is supported this year by the National Science Foundation in cooperation with the U.S. Atomic Energy Commission and the U.S. Air Force, Air Research and Development Command.

■ Recent research on the physics and chemistry of mercury and its compounds and their industrial and medical uses will be the subject of a 2-day meeting of the New York Academy of Sciences 6 and 7 Apr., at the Barbizon-Plaza Hotel.

A session on physics and chemistry, under the chairmanship of Frank C. Collins, professor of physical chemistry, Polytechnic Institute of Brooklyn, is scheduled from 9 A.M. to noon Friday, 6 Apr.; a session on pharmacology and toxicology will be held that afternoon from 2 to 5 P.M., with Carroll Handley, chairman of the department of pharmacology, Baylor University College of Medicine, Houston, Texas, as chairman; and a session on clinical medicine is scheduled for 9 A.M. to noon on 7 Apr., chaired by Harry Gold, professor of clinical pharmacology, Cornell University College of Medicine, New York City.

■ The ninth session of the Statistical Commission of the United Nations, one of the eight functional commissions of the Economic and Social Council, is to be held at U.N. headquarters in New York 16 Apr.–4 May. Among the items on the agenda for this session are the following: general survey of developments in international statistics; statistics of capital formation; classification of government financial accounts; balance of payments statistics; external trade statistics; minimum program of economic and social statistics; and national accounts.

■ Henry F. Holland, Assistant Secretary of State for Inter-American Affairs, was chairman of the United States delegation to the Inter-American Specialized Conference on Conservation of Natural Resources: The Continental Shelf and Marine Waters, which opened in Ciudad Trujillo, Dominican Republic, on 15 Mar.

Other delegates were William C. Herrington, special assistant for Fisheries and Wildlife, Department of State; Ralph L. Miller, chief of the Fuels Division, U.S. Geological Survey; and William Sanders, United States representative on the Inter-American Council of Jurists.

The meeting was called pursuant to a resolution of the tenth Inter-American Conference at Caracas, Venezuela, in March 1954, for the purpose of studying various juridical, economic, and scientific problems related to the continental shelf and ocean waters of the Western Hemisphere.

■ The Ergonomics Research Society will hold a symposium on "Human factors in road transport," at the University of Bristol, 16–19 Apr. Inquiries about the program should be directed to H. Murrell, The Miners' Arms, Priddy, Wells, Somerset, England.

■ The 28th annual field meeting of the New York State Geological Association will be held at the University of Rochester, 4–6 May 1956. Field excursions will cover the stratigraphy, paleontology, geomorphology, and economic geology of Silurian-Devonian rocks and Pleistocene deposits. For further information, write W. R. Evitt, department of geology, University of Rochester, Rochester 3, N.Y. or K. E. Lowe, Department of Geology, The City College, New York 31.

## Forthcoming Events

### April

*28–5.* International Conf. on Health Education, 3rd, Rome, Italy. (L. Viborel, International Union for Health Education of the Public, Paris, 1er, France.)

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*29–3.* Semiconductor Symposium of Electrochemical Soc., 4th annual, San Francisco, Calif. (J. W. Faust, Jr., Westinghouse Research Laboratories, Beulah Rd., Pittsburgh 35, Pa.)

*29–3.* Southwestern and Rocky Mountain Div., AAAS, annual, Las Cruces, N.M. (F. E. E. Germann, Dept. of Chemistry, Univ. of Colorado, Boulder.)

*29–4.* Soc. of American Bacteriologists, annual, Houston, Tex. (J. H. Bailey, Sterling-Winthrop Research Inst., Rensselaer, N.Y.)

*29–4.* Soc. of Motion Picture and Television Engineers, 79th, New York, N.Y. (SMPTE, 55 W. 42 St., New York 36.)

*30–2.* American Geophysical Union, annual, Washington, D.C. (W. E. Smith, AGU, 1530 P St., NW, Washington 5.)

*30–3.* International Scientific Radio Union, spring meeting, Washington, D.C. (J. P. Hagen, 2101 Constitution Ave., NW, Washington 25.)

*30–3.* International Symposium on Rheumatic Fever, 1st, Mexico City, Mexico. (SIBIC, Av. Cuauhtémoc 300, México 7, D. F.)

*30–4.* American Meteorological Soc., Washington, D.C. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)

*30–4.* American Psychiatric Assoc., annual, Chicago, Ill. (D. Blain, APA, 1785 Massachusetts Ave., NW, Washington 6.)

### May

*1–3.* Electronic Components Symposium, 7th annual, Washington, D.C. (A. W. Rogers, U.S. Army Signal Corps, Fort Monmouth, N.J.)

*3–5.* American Philosophical Assoc., Western Div., Bloomington, Ind. (W. H. Hay, Bascom Hall, Univ. of Wisconsin, Madison 6.)

*3–5.* Illinois State Acad. of Science, annual, Springfield, Ill. (L. E. Bamber, 223 Natural History, Univ. of Illinois, Urbana.)

*3–5.* Midwestern Psychological Assoc., annual, St. Louis, Mo. (D. W. Fiske, Dept. of Psychology, Univ. of Chicago, Chicago 37, Ill.)

*3–5.* Soc. for American Archaeology, annual, Lincoln, Nebr. (A. C. Spaulding, Museum of Anthropology, Univ. of Michigan, Ann Arbor.)

*4.* American Assoc. of Spectrographers, 7th annual, Chicago, Ill. (J. P. Merutka, H. M. Harper Co., 8200 Lehigh Ave., Morton Grove, Ill.)

*4.* Annual Conf. for Engineers, Columbus, Ohio. (H. A. Bolz, College of Engineering, Ohio State Univ., Columbus 10.)

*4–5.* Minnesota Acad. of Science, annual, Minneapolis. (B. O. Krogstad, Science and Mathematics Div., Univ. of Minnesota, Duluth Branch. Duluth 5.)

*4–5.* Wisconsin Acad. of Sciences, Arts, and Letters, annual, Milwaukee. (R. J. Dicke, 3 King Hall, Univ. of Wisconsin, Madison 6.)

*4–6.* Oklahoma Acad. of Science, Quartz Mountain State Park. (D. E. Howell, Entomology Dept., Oklahoma A. & M. College, Stillwater.)

*6–9.* American Inst. of Chemical Engineers, New Orleans, La. (F. J. Van Antwerpen, AIChE, 25 W. 45 St., New York 36.)

*7–8.* New Orleans Acad. of Science, annual, New Orleans, La. (Father J. H. Mullahy, S.J., Dept. of Biological Sciences, Loyola Univ., New Orleans 18.)

*9.* American Acad. of Arts and Sciences, annual, Cambridge, Mass. (R. W. Burhoe, 28 Newbury St., Boston 16, Mass.)

*9–12.* Virginia Acad. of Science, annual, Richmond, Va. (F. F. Smith, Box 1420, Richmond 11.)

*10.* Assoc. of Vitamin Chemists, Chicago, Ill. (M. Freed, Dawes Products, 4800 S. Richmond, Chicago 32.)

*10–11.* American Inst. of Chemists, annual, Boston, Mass. (L. Van Doren, AIC, 60 E. 42 St., New York 17.)

*10–11.* Atomic Energy Conf., San Antonio, Tex. (E. Wiggin, Atomic Industrial Forum, Inc., 260 Madison Ave., New York 16.)

*10–11.* Operations Research Soc. of America, 4th annual, Washington, D.C. (H. J. Miser, Rt. 2, Box 211, Vienna, Va.)

*10–12.* National Science Fair, 7th annual, Oklahoma City, Okla. (J. H. Kraus, Science Clubs of America, 1719 N St., NW, Washington 6.)

*11–12.* Indiana Acad. of Science, Martinsville. (W. A. Daily, Eli Lilly Research Laboratories, Indianapolis 6, Ind.)

*14–15.* Soc. of American Military Engineers, 36th annual, Washington, D.C. (SAME, 808 Mills Bldg., Washington 6.)

*14–19.* Assoc. of Official Seed Analysts, Sacramento, Calif. (R. G. Colborn, Seed Div., Dept. of Agriculture, Capitol Bldg., Lincoln, Nebr.)

*14–19.* International Spectroscopical Colloquium, 6th, Amsterdam. (F. Freese, Laboratorium voor Analytische Chemie, 125 Nieuwe Achtergracht, Amsterdam.)

*15–16.* Industrial Nuclear Technology Conf., Chicago, Ill. (INT Conf., Armour Research Foundation, 10 W. 35 St., Chicago 16.)

*16–18.* American College of Cardiology, 5th annual, Chicago, Ill. (P. Reichert, Empire State Bldg., New York, N.Y.)

*(See issue of 16 March for comprehensive list)*

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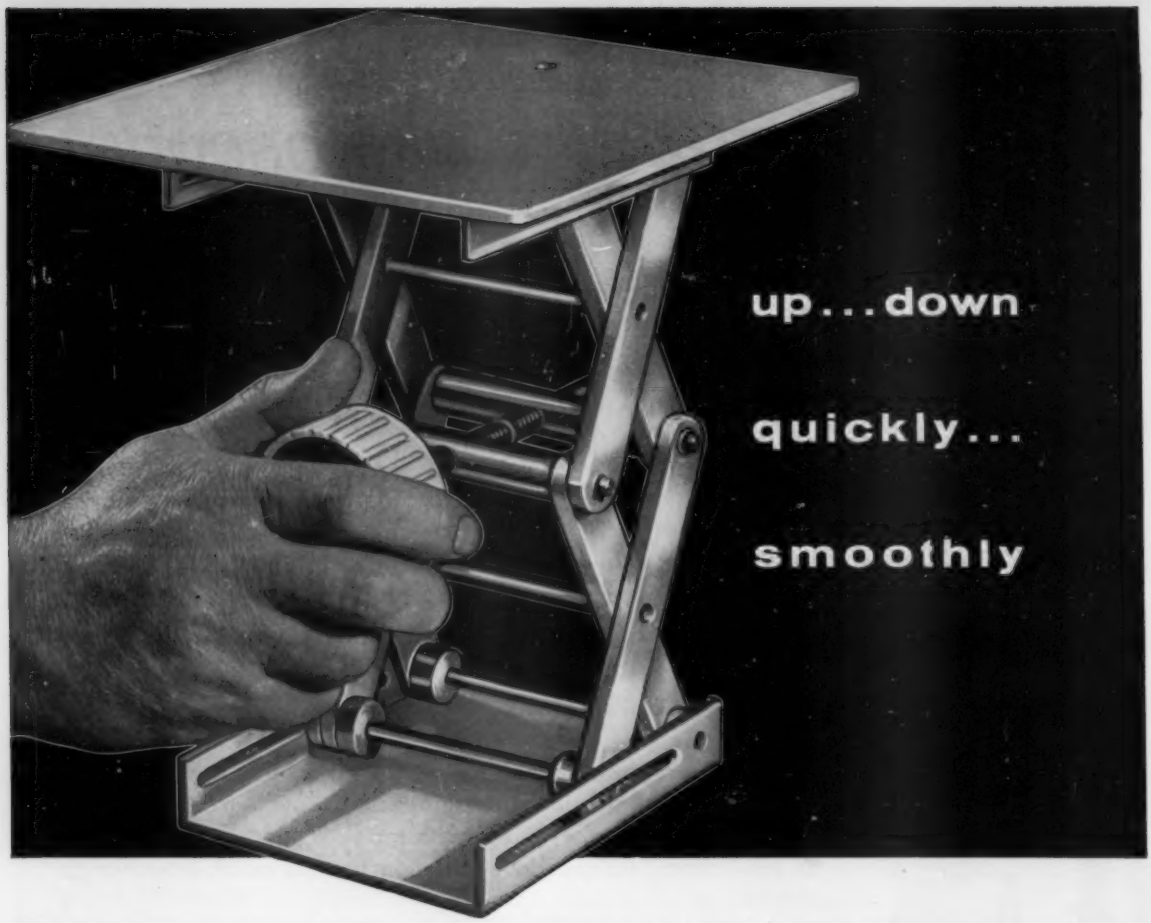


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